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FILE 'HOME' ENTERED AT 15:14:04 ON 11 DEC 2000

=> b medline caplus lifesci embase uspatfull

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=> s ascobate and promoter

L1 2 ASCOBATE AND PROMOTER

=> s ascorbate and promoter

L2 671 ASCORBATE AND PROMOTER

=> dup rem l1

PROCESSING COMPLETED FOR L1

L3 2 DUP REM L1 (0 DUPLICATES REMOVED)

=> d l3 ibib abs tot

L3 ANSWER 1 OF 2 USPATFULL

ACCESSION NUMBER: 2000:146555 USPATFULL

TITLE: Non-endogenous, constitutively activated human
 serotonin receptors and small molecule modulators
 thereof

INVENTOR(S): Behan, Dominic P., San Diego, CA, United States
 Chalmers, Derek T., Solana Beach, CA, United States
 Foster, Richard J., Cornwall, United Kingdom
 Glen, Robert C., Glencoe, MO, United States
 Lawless, Michael S., St. Charles, MO, United States
 Liaw, Chen W., San Diego, CA, United States
 Liu, Qian, Ballwin, MO, United States
 Russo, Joseph F., San Diego, CA, United States
 Smith, Julian R., Devon, United Kingdom
 Thomsen, William J., Del Mar, CA, United States

PATENT ASSIGNEE(S): Arena Pharmaceuticals, Inc., San Diego, CA, United
 States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6140509	20001031
APPLICATION INFO.:	US 1999-292069	19990414 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-90783	19980626 (60)
	US 1998-112909	19981218 (60)
	US 1999-123000	19990305 (60)

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Ramsuer, Robert W.

LEGAL REPRESENTATIVE: Woodcock Washburn Kurtz Mackiewicz & Norris LLP

NUMBER OF CLAIMS: 1

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 29 Drawing Figure(s); 17 Drawing Page(s)

LINE COUNT: 3319

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A compound of formula (C) useful as a serotonin receptor modulator

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 2 OF 2 USPATFULL

ACCESSION NUMBER: 2000:109829 USPATFULL
TITLE: 5-HT2A receptor inverse agonists
INVENTOR(S): Behan, Dominic P., San Diego, CA, United States
Chalmers, Derek T., Solana Beach, CA, United States
Foster, Richard J., Cornwall, United Kingdom
Glen, Robert C., Glencoe, MO, United States
Lawless, Michael S., St. Charles, MO, United States
Liaw, Chen W., San Diego, CA, United States
Liu, Qian, Ballwin, MO, United States
Russo, Joseph F., San Diego, CA, United States
Smith, Julian R., Devon, United Kingdom
Thomsen, William J., Del Mar, CA, United States
PATENT ASSIGNEE(S): Arena Pharmaceuticals Inc., San Diego, CA, United States (U.S. corporation)
Tripos, Inc., St. Louis, MO, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6107324	20000822
APPLICATION INFO.:	US 1999-292071	19990414 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1998-60188, filed on 14 Apr 1998	

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-90783	19980626 (60)
	US 1998-112909	19981218 (60)
	US 1999-123000	19990305 (60)
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Jarvis, William R. A.	
LEGAL REPRESENTATIVE:	Woodcock, Washburn, Kurtz, Mackiewicz & Norris, LLP; Burgoon, Jr., Richard P.	
NUMBER OF CLAIMS:	7	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	24 Drawing Figure(s); 17 Drawing Page(s)	
LINE COUNT:	3501	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		
AB	Disclosed herein is a new class of pyrazole compounds which act at the 5HT.sub.2A receptors.	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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FILE 'MEDLINE, CAPLUS, LIFESCI, EMBASE, USPATFULL' ENTERED AT 15:14:47
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L1 2 S ASCOBATE AND PROMOTER
L2 671 S ASCORBATE AND PROMOTER
L3 2 DUP REM L1 (0 DUPLICATES REMOVED)

=> s 12 and reproter

L4 0 L2 AND REPROTER

=> s 12 and reporter

L5 45 L2 AND REPORTER

=> dup rem 15

PROCESSING COMPLETED FOR L5

L6 40 DUP REM L5 (5 DUPLICATES REMOVED)

=> d l6 ibib abs 1-10

L6 ANSWER 1 OF 40 USPATFULL

ACCESSION NUMBER: 2000:146512 USPATFULL
TITLE: Zinc finger protein derivatives and methods therefor
INVENTOR(S): Barbas, III, Carlos F., San Diego, CA, United States
Gottesfeld, Joel M., Del Mar, CA, United States
Wright, Peter E., La Jolla, CA, United States
PATENT ASSIGNEE(S): The Scripps Research Institute, La Jolla, CA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6140466	20001031
APPLICATION INFO.:	US 1997-863813	19970527 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 676318	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Achutamurthy, Ponnathapu	
ASSISTANT EXAMINER:	Moore, William W.	
LEGAL REPRESENTATIVE:	Gray Cary Ware & Freidenrich LLP; Haile, Lisa A.	
NUMBER OF CLAIMS:	54	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	32 Drawing Figure(s); 26 Drawing Page(s)	
LINE COUNT:	4196	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Zinc finger proteins of the Cys.sub.2 His.sub.2 type represent a class of malleable DNA binding proteins which may be selected to bind diverse sequences. Typically, zinc finger proteins containing three zinc finger domains, like the murine transcription factor Zif268 and the human transcription factor Spl, bind nine contiguous base pairs (bp). To create a class of proteins which would be generally applicable to target unique sites within complex genomes, the present invention provides a polypeptide linker that fuses two three-finger proteins. Two six-fingered proteins were created and demonstrated to bind 18 contiguous bp of DNA in a sequence specific fashion. Expression of these proteins as fusions to activation or repression domains allows transcription to be specifically up or down modulated within cells. Polydactyl zinc finger proteins are broadly applicable as genome-specific transcriptional switches in gene therapy strategies and the development of novel transgenic plants and animals. Such proteins are useful for inhibiting, activating or enhancing gene expression from a zinc finger-nucleotide binding motif containing **promoter** or other transcriptional control element, as well as a structural gene or RNA sequence.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 2 OF 40 USPATFULL

ACCESSION NUMBER: 2000:142119 USPATFULL
TITLE: High-affinity salicylic acid-binding protein and methods of use
INVENTOR(S): Klessig, Daniel F., Bridgewater, NJ, United States
Du, He, Piscataway, NJ, United States
PATENT ASSIGNEE(S): Rutgers, The State University of New Jersey, New Brunswick, NJ, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6136552	20001024
APPLICATION INFO.:	US 1997-956507	19971023 (8)

	NUMBER	DATE
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PRIORITY INFORMATION:	US 1996-29806	19961025 (60)
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Housel, James C.	
ASSISTANT EXAMINER:	Portner, Ginny Allen	
LEGAL REPRESENTATIVE:	Dann, Dorfman, Herrell and Skillman	
NUMBER OF CLAIMS:	7	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	12 Drawing Figure(s); 11 Drawing Page(s)	
LINE COUNT:	1199	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A high-affinity salicylic acid-binding protein (SABP2) derivable from tobacco and Arabidopsis is disclosed. The tobacco protein has a molecular weight of approximately 25 kDa and reversibly binds SA with an apparent K_{sub}.d of approximately 90 nM and a B_{sub}.max of 10 fmol/mg protein. The SABP2 of the invention may be used to identify analogues of SA. Analogues so identified may be used in plants to augment disease-resistance response pathways or other SA-sensitive processes in which SA plays a role. Possible examples include flowering and alternative respiration. The SABP2 of the invention may also be used to identify and clone a gene or cDNA that encodes it, which then may be used to generate transgenic plants having altered SABP2 levels.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 3 OF 40 USPATFULL

ACCESSION NUMBER: 2000:138116 USPATFULL
 TITLE: Condensed plasmid-liposome complex for transfection
 INVENTOR(S): Huang, Shi Kun, Castro Valley, CA, United States
 Oto, Edwin Kiyoshi, Redwood City, CA, United States
 Hassanipour, Mohammad, Vallejo, CA, United States
 Jin, Bei, Union City, CA, United States
 PATENT ASSIGNEE(S): Sequus Pharmaceuticals, Inc., Menlo Park, CA, United States (U.S. corporation)

	NUMBER	DATE
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PATENT INFORMATION:	US 6133026	20001017
APPLICATION INFO.:	US 1998-151436	19980911 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1997-827236, filed on 28 Mar 1997, now patented, Pat. No. US 5851818	

which is a continuation-in-part of Ser. No. US 1996-657795, filed on 31 May 1996, now abandoned

DOCUMENT TYPE: Utility
 PRIMARY EXAMINER: Schwartzman, Robert A.
 ASSISTANT EXAMINER: Shuman, Jon
 LEGAL REPRESENTATIVE: Mohr, Judy M. Dehlinger & Associates
 NUMBER OF CLAIMS: 14
 EXEMPLARY CLAIM: 1
 NUMBER OF DRAWINGS: 36 Drawing Figure(s); 13 Drawing Page(s)
 LINE COUNT: 995

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A plasmid-liposome composition for transfection of a cell is described. The composition includes plasmid molecules condensed with a polycationic condensing agent and cationic liposomes. Also disclosed is a method for preparing the plasmid-liposome complexes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 4 OF 40 USPATFULL

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-43852	19970411 (60)
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Lambkin, Deborah C.	
LEGAL REPRESENTATIVE:	Schwegman, Lundberg, Woessner & Kluth, P.A.	
NUMBER OF CLAIMS:	18	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	13 Drawing Figure(s); 14 Drawing Page(s)	
LINE COUNT:	4129	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides a method of treating a mammal having, or at risk of, an indication associated with a TGF-beta deficiency comprising administering one or more agents that is effective to elevate the level of TGF-beta. The invention also provides novel compounds that elevate TGF-beta levels, as well as pharmaceutical compositions comprising compounds that elevate TGF-beta levels, and methods for detecting diseases associated with endothelial cell activation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 6 OF 40 USPATFULL

ACCESSION NUMBER: 2000:113489 USPATFULL
TITLE: Methods of using morphogen analogs
INVENTOR(S): Sampath, Kuber T., Medway, MA, United States
PATENT ASSIGNEE(S): Creative BioMolecules, Inc., Boston, MA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6110460	20000829
APPLICATION INFO.:	US 1997-872859	19970611 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1995-507750, filed on 26 Jul 1995, now patented, Pat. No. US 5932716, issued on 3 Aug 1999	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Clark, Deborah J.	
LEGAL REPRESENTATIVE:	Elrifi, Ivor R.; Morency, MichelMintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.	
NUMBER OF CLAIMS:	5	
EXEMPLARY CLAIM:	1,2	
NUMBER OF DRAWINGS:	12 Drawing Figure(s); 12 Drawing Page(s)	
LINE COUNT:	1733	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed herein are methods and compositions for identifying morphogen analogs. Preferred methods rest on the use of test cells comprising DNA defining a morphogen-responsive transcription activating element operatively associated with a **reporter** gene. In certain embodiments, the methods involve an osteogenic protein 1 (OP-1) responsive transcription activating element. Substances that activate the OP-1 responsive transcription activating element are considered herein likely to be useful for reproducing in vivo effects of morphogens such as OP-1.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 7 OF 40 USPATFULL

ACCESSION NUMBER: 2000:106138 USPATFULL
TITLE: Polyhydroxyalkanoate synthesis in plants
INVENTOR(S): Srienc, Friedrich, Lake Elmo, MN, United States
Somers, David A., Roseville, MN, United States
Hahn, J. J., New Brighton, MN, United States
Eschenlauer, Arthur C., Circle Pines, MN, United States

PATENT ASSIGNEE(S): Regents of the University of Minnesota, Minneapolis,
MN, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6103956	20000815
APPLICATION INFO.:	US 1998-52607	19980331 (9)
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Smith, Lynette R. F.	
ASSISTANT EXAMINER:	Nelson, Amy J.	
LEGAL REPRESENTATIVE:	Muetting, Raasch & Gebhardt, P.A.	
NUMBER OF CLAIMS:	30	
EXEMPLARY CLAIM:	28	
NUMBER OF DRAWINGS:	17 Drawing Figure(s); 9 Drawing Page(s)	
LINE COUNT:	2757	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel transgenic plants and plant cells are capable of biosynthesis of polyhydroxyalkanoate (PHA). Heterologous enzymes involved in PHA biosynthesis, particularly PHA polymerase, are targeted to the peroxisome of a transgenic plant. Transgenic plant materials that biosynthesize short chain length monomer PHAs in the absence of heterologous .beta.-ketothiolase and acetoacetyl-CoA reductase are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 8 OF 40 USPATFULL

ACCESSION NUMBER: 2000:105676 USPATFULL
TITLE: Methods and compositions for identifying morphogen analogs
INVENTOR(S): Sampath, Kuber T., Holliston, MA, United States
PATENT ASSIGNEE(S): Creative BioMolecules, Inc., Boston, MA, United States
(U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6103491	20000815
APPLICATION INFO.:	US 1996-764528	19961212 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1995-507750, filed on 26 Jul 1995, now patented, Pat. No. US 5932716	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Kemmerer, Elizabeth	
LEGAL REPRESENTATIVE:	Elrifi, Ivor R.; Moreney, MichelMintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.	
NUMBER OF CLAIMS:	12	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	12 Drawing Figure(s); 12 Drawing Page(s)	
LINE COUNT:	2706	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed herein are methods and compositions for identifying morphogen analogs. The preferred methods and compositions relate to the discovery that morphogen upregulation of the mouse type X collagen **promoter** activity is mediated by a MEF-2 like sequence and required an adjacent AP-1 sequence. Certain methods rest on the use of test cells comprising DNA defining a morphogen-responsive transcription activating element operatively associated with a **reporter** gene. Other methods rest on the use of DNAs for measuring morphogen-inducible DNA-binding. In certain preferred embodiments, the methods and DNAs involve an osteogenic protein 1 (OP-1) responsive transcription activating element. Substances that mediate interaction with and/or activate the OP-1 responsive transcription activating element are considered herein likely to be useful for reproducing in vivo effects of morphogens such as OP-1.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 9 OF 40 USPATFULL

ACCESSION NUMBER: 2000:102483 USPATFULL
TITLE: Pathogen-inducible regulatory element
INVENTOR(S): Chappell, Joseph, Lexington, KY, United States
Cornett, Catherine A. G., Lexington, KY, United States
Yin, Shaohui, Lexington, KY, United States
PATENT ASSIGNEE(S): Board of Trustees of the University of Kentucky,
Lexington, KY, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6100451	20000808
APPLICATION INFO.:	US 1995-577483	19951222 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1995-471983, filed on 6 Jun 1995, now abandoned which is a continuation of Ser. No. US 1995-443639, filed on 18 May 1995	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Robinson, Douglas W.	
ASSISTANT EXAMINER:	Nelson, Amy J.	
LEGAL REPRESENTATIVE:	Clark & Elbing LLP	
NUMBER OF CLAIMS:	54	
EXEMPLARY CLAIM:	1,54	
NUMBER OF DRAWINGS:	25 Drawing Figure(s); 12 Drawing Page(s)	
LINE COUNT:	2398	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Qualitative transcriptional regulatory sequences functional in plants, plant tissue and in plant cells for inducible gene expression and quantitative transcriptional regulatory sequences for increasing the transcriptional expression of downstream genetic information in plants, plant tissue and plant cells are disclosed. Also disclosed are methods and recombinant DNA molecules for improving the disease resistance of transgenic plants, especially wherein an inducible **promoter** controls the expression of a protein capable of evoking the hypersensitive response in a plant.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 10 OF 40 USPATFULL

ACCESSION NUMBER: 2000:91699 USPATFULL
TITLE: Methods and compositions for identifying morphogen analogs
INVENTOR(S): Harada, Shun-ichi, North Wales, PA, United States
Rodan, Gideon A., Bryn Mawr, PA, United States
Sampath, Kuber T., Holliston, MA, United States
PATENT ASSIGNEE(S): Creative BioMolecules, Inc., Hopkington, MA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6090544	20000718
APPLICATION INFO.:	US 1996-764522	19961212 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1995-507598, filed on 26 Jul 1995	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Railey, II, Johnny F.	
LEGAL REPRESENTATIVE:	Morency, Michel; Elrifi, Ivor R.Mintz, Levin, et al.	
NUMBER OF CLAIMS:	9	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	12 Drawing Figure(s); 12 Drawing Page(s)	
LINE COUNT:	2684	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed herein are methods and compositions for identifying morphogen analogs. The preferred methods and compositions relate to the discovery that morphogen upregulation of the mouse type X collagen **promoter** activity is mediated by a MEF-2 like sequence and

requires an adjacent AP-1 sequence. Certain methods rest on the use of test cells comprising DNA defining a morphogen-responsive transcription activating element operatively associated with a **reporter** gene. Other methods rest on the use of DNAs for measuring morphogen-inducible DNA-binding. In certain preferred embodiments, the methods and DNAs involve an osteogenic protein 1 (OP-1) responsive transcription activating element. Substances that mediate interaction with and/or activate the OP-1 responsive transcription activating element are considered herein likely to be useful for reproducing in vivo effects of morphogens such as OP-1.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L1 2 S ASCORBATE AND PROMOTER
L2 671 S ASCORBATE AND PROMOTER
L3 2 DUP REM L1 (0 DUPLICATES REMOVED)
L4 0 S L2 AND REPROTER
L5 45 S L2 AND REPORTER
L6 40 DUP REM L5 (5 DUPLICATES REMOVED)

=> s ascorbate (p) promoter

L7 229 ASCORBATE (P) PROMOTER

=> s l7 (p) reporter

L8 7 L7 (P) REPORTER

=> dup rem l8

PROCESSING COMPLETED FOR L8

L9 2 DUP REM L8 (5 DUPLICATES REMOVED)

=> d l9 ibib abs tot

L9 ANSWER 1 OF 2 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000058358 MEDLINE
DOCUMENT NUMBER: 20058358
TITLE: Direct observation of stress response in Caenorhabditis elegans using a reporter transgene.
AUTHOR: Link C D; Cypser J R; Johnson C J; Johnson T E
CORPORATE SOURCE: Institute for Behavioral Genetics, University of Colorado Boulder 80309-0447, USA.. linkc@colorado.edu
CONTRACT NUMBER: AG12423 (NIA)
PO1-AG08761 (NIA)
KO2-AA00195 (NIAAA)
+
SOURCE: CELL STRESS AND CHAPERONES, (1999 Dec) 4 (4) 235-42.
Journal code: CV5. ISSN: 1355-8145.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY WEEK: 20000204
AB Transgenic Caenorhabditis elegans expressing jellyfish Green Fluorescent

Protein under the control of the **promoter** for the inducible small heat shock protein gene hsp-16-2 have been constructed. Transgene expression parallels that of the endogenous hsp-16 gene, and, therefore, allows direct visualization, localization, and quantitation of hsp-16 expression in living animals. In addition to the expected upregulation by heat shock, we show that a variety of stresses, including exposure to superoxide-generating redox-cycling quinones and the expression of the human beta amyloid peptide, specifically induce the **reporter** transgene. The quinone induction is suppressed by coincubation with L-**ascorbate**. The ability to directly observe the stress response in living animals significantly simplifies the identification of both exogenous treatments and genetic alterations that modulate stress response, and possibly life span, in *C. elegans*.

L9 ANSWER 2 OF 2 MEDLINE DUPLICATE 2
 ACCESSION NUMBER: 97354114 MEDLINE
 DOCUMENT NUMBER: 97354114
 TITLE: Cloning of the pumpkin ascorbate oxidase gene and analysis of a cis-acting region involved in induction by auxin.
 AUTHOR: Kisu Y; Harada Y; Goto M; Esaka M
 CORPORATE SOURCE: Faculty of Applied Biological Science, Hiroshima University, Higashi-Hiroshima, Japan.
 SOURCE: PLANT AND CELL PHYSIOLOGY, (1997 May) 38 (5) 631-7.
 Journal code: B1G. ISSN: 0032-0781.
 PUB. COUNTRY: Japan
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 OTHER SOURCE: GENBANK-D55677
 ENTRY MONTH: 199710
 ENTRY WEEK: 19971003

AB A genomic clone encoding **ascorbate** oxidase was isolated from pumpkin (*Cucurbita* sp.). This gene is consisted of four exons and three introns. Analyses of the **promoter** fusion to beta-glucuronidase **reporter** gene by transient expression assay in pumpkin fruit tissues suggested the existence of a cis-acting region responsible for auxin regulation.

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ON

11 DEC 2000

L1 2 S ASCORBATE AND PROMOTER
 L2 671 S ASCORBATE AND PROMOTER
 L3 2 DUP REM L1 (0 DUPLICATES REMOVED)
 L4 0 S L2 AND REPROTER
 L5 45 S L2 AND REPORTER
 L6 40 DUP REM L5 (5 DUPLICATES REMOVED)
 L7 229 S ASCORBATE (P) PROMOTER
 L8 7 S L7 (P) REPORTER
 L9 2 DUP REM L8 (5 DUPLICATES REMOVED)

=> s l7 and reporter

L10 8 L7 AND REPORTER

=> s l10 not l8

L11 1 L10 NOT L8

=> d l11 ibib abs kwic

L11 ANSWER 1 OF 1 USPATFULL

ACCESSION NUMBER: 2000:5020 USPATFULL

TITLE: Molecular methods of hybrid seed production

INVENTOR(S): Fabijanski, Steven F., Ontario, Canada

Albani, Diego, Norfolk, United Kingdom

Robert, Laurian S., Ottawa, Canada

Arnison, Paul G., Ontario, Canada

PATENT ASSIGNEE(S): Pioneer Hi-Bred International, Inc., Des Moines, IA,
United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6013859	20000111
APPLICATION INFO.:	US 1995-476864	19950607 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1994-276510, filed on 14 Jul 1994 which is a continuation of Ser. No. US 556917	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Fox, David T.	
LEGAL REPRESENTATIVE:	Foley & Lardner	
NUMBER OF CLAIMS:	23	
EXEMPLARY CLAIM:	1,11	
NUMBER OF DRAWINGS:	30 Drawing Figure(s); 78 Drawing Page(s)	
LINE COUNT:	4621	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A process is described for producing fertile hybrid seed or hybrid seed
comprising fertile and sterile seed using male-sterile plants created
by
employing molecular techniques to manipulate genes that are capable of
controlling the production of fertile pollen in plants. Hybrid seed
production is simplified and improved by this approach, which can be
extended to plant crop species for which commercially acceptable hybrid
seed production methods have not been available.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . development and/or function gene is expressed, a similar
series

of analyses can be carried out using as a probe a **reporter**
gene such as beta-glucuronidase joined to the promoter essential for
pollen development and/or function, or a native gene from the. . .

is
isolated from one plant and used in a different plant species the
preferred method is the use of a **reporter** gene joined to the
promoter to determine the exact developmental timing that the promoter
has in that particular plant species.

DETD . . . one DNA sequence in the recombinant DNA molecule the
expression

of the DNA sequences may be regulated by an identical **promoter**
or the expression of each DNA sequence may be regulated by a different
promoter. Preferably, the expression of the DNA sequences is
regulated by a **promoter** essential for pollen development
and/or function as hereinbefore described so that the gene product

which

renders a non-toxic substance cytotoxic. . . a non-toxic substance,
the expression of the DNA sequence and the second DNA sequence may be
regulated by either a **promoter** essential for pollen
development and/or function, an inducible **promoter** or a
constitutive **promoter** so long as there is selective
interference with the function and/or development of cells essential to
pollen formation and/or function.. . the expression of the DNA
sequence encoding a gene product which renders a non-toxic substance
cytotoxic is regulated by a **promoter** essential for pollen
development and/or function and the expression of the second DNA
sequence encoding a gene product which converts a substance which is
endogenous to the cell to a non-toxic substance is regulated by a

constitutive **promoter**, an inducible **promoter** or a **promoter** essential for pollen development and/or function, although most preferably by a **promoter** essential for pollen development and/or function. For a more detailed discussion of the above-mentioned promoters reference may be made to the discussion of promoters in reference to the recombinant DNA molecules containing anti-sense genes. A preferred **promoter** would be the microspore-specific Bp10 **promoter** (Albani, D., Sardana, R., Robert, L. S., Altosaar, I., Arnison, P. G., and Fabijanski, S. F., A Brassica napus gene family which shows sequence similarity to ascorbate oxidase is expressed in developing pollen. Molecular characterization and analysis of **promoter** activity in transgenic tobacco plants. Plant J. 2:331-342 (1992) or the anther-specific TA39 **promoter** hereinbefore described.

DETD . . . anti-sense vector PAL1302 is shown. A plasmid containing the GUS gene (Beta-glucuronidase, described in Jefferson, R. A., Plant Molecular Biology **Reporter**, 1987, 5:387-405) in the anti-sense orientation flanked by the CaMV 35S promoter and the nos termination signal was obtained from. . .

DETD The construction of pollen specific vectors that utilize the **promoter** regions of clones L10 and L19 was conducted as follows. The construction of the pollen specific vectors depicted in FIG. 8 utilizes **promoter** regions from clone L10. The start of transcription of clone L10 is located at nucleotide 1. The ATG start codon is located at nucleotides 45-47. The **promoter** region of this clone was excised by first subcloning the EcoRI-XbaI fragment of the clone that encompasses the entire **promoter** region and a portion of the first exon (the XbaI site is nucleotide 358 in the DNA sequence). This subclone. . . a DNA fragment of 459 nucleotides

which contains 62 nucleotides of untranslated transcribed leader sequence, and

397 nucleotides of 5' **promoter** region. The NdeI site in this fragment was made blunt ended by the use of Klenow, and this fragment was. . . Clones were recovered in both orientations and the clone that contained the fragment in the orientation: HindIII, SphI, PstI, HincII, **promoter**-62 base pair leader fragment (NdeI blunt/HincII, does not cut with either HincII or NdeI) XbaI, BamHI, SmaI, KpnI, SstI, EcoRI. . . I, made blunt end by the use of Klenow, then digested with EcoRI. To this cut subclone was added the **promoter**/untranslated leader sequence of pPAL1020 by digesting pPAL1020 with HincII and EcoRI, and adding this **promoter** fragment to the cut pPAL10Hc. The resultant subclone contained a reconstructed **promoter** region of clone L10 differing from the intact region by only the filled in KpnI site used for the joining of the two **promoter** fragments. This construct was named pPAL1021. This vector contains in the following order: HindIII, PstI, SphI, HincII, SalI, XbaI, BamHI, the approximately 1 Kb HincII fragment

joined to the HincII-NdeI **promoter** fragment followed by XbaI, BamHI, SmaI, KpnI, SstI, and EcoRI. This subclone allows for the convenient removal of the **promoter** region of clone L10 such that the **promoter** can be easily used in cassette transformation vectors. The outline of this construction is shown in FIG. 8. The **promoter** region of pPAL1021 was used for the construction of a pollen specific cassette transformation vector by carrying out the following. . . was treated with Klenow and relegated. This procedure effectively removed the portion of the polylinker that was 5' to the **promoter** in pPAL1021. This plasmid was then digested with HindIII and SstI, and cloned into the HindIII and SstI sites of PAL1001,

giving rise to PAL1121. PAL1121 has in the following order: the **promoter** essential for pollen development and/or function of clone L10 (approximately 1.1-1.2 Kb), followed by a polylinker with the following unique. . . BamHI, SmaI, KpnI, SstI, followed by the nos ter. The construction of this is outlined in FIG. 8. The L10

promoter isolated here is also referred to as **promoter** Bp10. Also see Albani, D., Sardana, R., Robert, L. S., Altosaar, I., Arnison, P. G., and Fabijanski, S. F., A Brassica napus gene family which shows sequence similarity to **ascorbate** oxidase is expressed in developing pollen. Molecular characterization and analysis of **promoter** activity in transgenic tobacco plants. Plant J. 2:331-342 (1992).

=> s ascorbate (s) promoter

L12 189 ASCORBATE (S) PROMOTER

=> dup rem l12

PROCESSING COMPLETED FOR L12

L13 108 DUP REM L12 (81 DUPLICATES REMOVED)

=> s l13 and induc?

L14 60 L13 AND INDUC?

=> d l14 ibib abs 1-10

L14 ANSWER 1 OF 60 MEDLINE

ACCESSION NUMBER: 2000216846 MEDLINE

DOCUMENT NUMBER: 20216846

TITLE: Significant overexpression of metallothionein and cyclin D1

and apoptosis in the early process of rat urinary bladder carcinogenesis **induced** by treatment with N-butyl-N-(4-hydroxybutyl)nitrosamine or sodium L-ascorbate.

AUTHOR: Takaba K; Saeki K; Suzuki K; Wanibuchi H; Fukushima S

CORPORATE SOURCE: Toxicological Research Laboratories, Kyowa Hakko Kogyo Co. Ltd, 2548 Fujimagari, Ube, Yamaguchi 755-8501, Japan.. katsumi.takaba@kyowa.co.jp

SOURCE: CARCINOGENESIS, (2000 Apr) 21 (4) 691-700. Journal code: C9T. ISSN: 0143-3334.

PUB. COUNTRY: ENGLAND: United Kingdom Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 200007

ENTRY WEEK: 20000704

AB Effects of a genotoxic bladder carcinogen, N-butyl-N-(4-hydroxybutyl)nitrosamine (BBN) and a non-genotoxic bladder **promoter**, sodium L-**ascorbate** (Na-AsA), on protein expression, cell proliferation and apoptosis of the bladder epithelium with or without the influence of testicular castration were investigated. Male F344 rats were divided into six groups (groups 1-6). BBN was given with 0.05% drinking water to groups 1 and 4 for 8 weeks, groups 2 and 5 received diet with 5% Na-AsA. Then the animals were treated without any chemicals. Groups 3 and 6 were non-treated controls. Testicular castration

was carried out 2 weeks before commencement of chemical treatment on groups 4-6. The total observation period was 18 weeks. Overexpression of cyclin D1 was **induced** by BBN but not Na-AsA and the degree of overexpression was higher in the order simple hyperplasia, papillary or nodular hyperplasia, papilloma and carcinoma. Metallothionein (MT) was also overexpressed in bladder epithelium treated with BBN but not Na-AsA, but was decreased in papillomas and never found in a carcinoma. Cyclin D1-positive cells were essentially MT-negative. Therefore, it is speculated that MT protects genes from insult by genotoxic carcinogens and

its lack is associated with tumor development. Apoptotic cell death occurred during treatment with BBN and Na-AsA and after their withdrawal. Chromatin condensation of many G0/G(1) cells was particularly marked on flow cytometry analysis 1 week after cessation of treatment, this being considered as an early apoptotic change. Although testicular castration had no influence on the above events, it resulted in decreased tumor formation as compared with the case of similarly treated intact animals. Our data demonstrate that overexpression of MT and cyclin D1 is specific for treatment with a genotoxic carcinogen, and suggest that MT overexpression may play an important suppressive role in the early stages of rat urinary bladder carcinogenesis.

L14 ANSWER 2 OF 60 MEDLINE

ACCESSION NUMBER: 2000152620 MEDLINE

DOCUMENT NUMBER: 20152620

TITLE: Antioxidative effect of melatonin on human spermatozoa.

AUTHOR: Gavella M; Lipovac V

CORPORATE SOURCE: Vuk Vrhovac Institute, University Clinic for Diabetes, Endocrinology and Metabolic Diseases, Medical Faculty University of Zagreb, Croatia.

SOURCE: ARCHIVES OF ANDROLOGY, (2000 Jan-Feb) 44 (1) 23-7.

Journal code: 69T. ISSN: 0148-5016.

PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200005

ENTRY WEEK: 20000502

AB The ability of melatonin to suppress experimentally induced lipid peroxidation (LPO) in sperm membrane was investigated in 41 samples of infertile men. Iron/**ascorbate** (0.04/0.2 mmol)-**induced** LPO was measured by the formation of malondialdehyde (MDA) using the thiobarbituric acid method. Sperm incubated in the presence of melatonin (2-6 mmol) exhibited a concentration-dependent decrease of MDA generated from hydroperoxide of the sperm plasma membrane in the presence of **promoter** system. Addition of 6 mmol of melatonin significantly reduced the rate of lipid peroxidation in sperm of unselected donors (mean +/- SE in control samples = 26.4 +/- 2.9 vs. 6.5 +/- 1.1 nmol MDA/10(8) sperm in melatonin-treated samples: n = 16, p < .005). Inhibitory effect of melatonin was also significant in the presence of 0.015 mmol of ferrous ions (20.5 +/- 1.7 vs. 7.9 +/- 1.6 nmol MDA/10(8) sperm in melatonin-treated samples: n = 7, p < .02) and (.005 mmol of ferrous ions (20.2 +/- 2.8 vs. 9.9 +/- 2.4 nmol MDA/ 10(8) sperm: n = 6, p < .05). Comparing the effect of melatonin with that of Trolox, an analog of vitamin E. a similar effect at concentration of 0.1-0.2 mmol of Trolox was found (25.2 +/- 2.9 vs. 11.8 +/- 1.2 nmol MDA/10(8) sperm in Trolox-treated samples: n = 7, p < .005). The obtained data of in vitro experiments show that melatonin is 40-fold less efficient than Trolox in achieving the 50% reduction in LPO (4 vs. 0.1 mmol). Since the physiological concentration of melatonin in human semen is at the nanomolar level, its antioxidative role in vivo is probably of minor importance.

L14 ANSWER 3 OF 60 MEDLINE

ACCESSION NUMBER: 2000142053 MEDLINE

DOCUMENT NUMBER: 20142053

TITLE: On the role of hydroxyl radical and the effect of tetrandrine on nuclear factor--kappaB activation by phorbol

12-myristate 13-acetate.

AUTHOR: Ye J; Ding M; Zhang X; Rojanasakul Y; Shi X

CORPORATE SOURCE: Pathology and Physiology Research Branch, Health Effects Laboratory Division, National Institute for Occupational

Safety and Health, Morgantown, West Virginia 25605, USA.
 * SOURCE: ANNALS OF CLINICAL AND LABORATORY SCIENCE, (2000 Jan) 30
 (1) 65-71.
 Journal code: 532. ISSN: 0091-7370.
 PUB. COUNTRY: United States
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200005
 ENTRY WEEK: 20000503
 AB Nuclear factor kappaB (NF-kappaB) is considered to be an important target for therapeutic intervention because of its role in the regulation of proinflammatory and profibrotic mediators. The present study examined the role of hydroxyl (*OH) radical and the effect of tetrandrine, an alkaloid extracted from the Chinese medicinal herb Stephania tetrandra, on NF-kappaB activation by a tumor **promoter**, phorbol 12-myristate 13-acetate (PMA) in human lymphoid T cells (ie, Jurkat cells). Exogenous superoxide dismutase (SOD) enhanced the NF-kappaB activation by PMA, while catalase blocked it. Formate, a scavenger of *OH radical, also was inhibitory, as was deferoxamine, a metal chelator. These data suggest an important role of *OH radical in PMA-**induced** NF-kappaB activation. Incubation of the cells with tetrandrine prior to the stimulation of the cells was found to inhibit PMA-**induced** NF-kappaB activation. Tetrandrine activity was so potent that 50 microm of tetrandrine was sufficient to inhibit activation of NF-kappaB completely. Electron spin resonance (ESR) spin trapping was used to investigate the antioxidant action of tetrandrine using 5,5-dimethyl-1-pyrroline N-oxide (DMPO) as a spin trap. Tetrandrine is an antioxidant for both *OH and superoxide (O2-) radicals. The reaction rate constant of tetrandrine with *OH is $1.4 \times 10^{10} \text{ M}^{-1} \text{ sec}^{-1}$, which is comparable with several well established antioxidants, such as **ascorbate**, glutathione, and cysteine. The Fenton reaction ($\text{Fe(II)} + \text{H}_2\text{O}_2 \rightarrow \text{Fe(III)} + * \text{OH} + \text{OH}^-$) and xanthine/xanthine oxidase were used as sources of *OH and O2- radicals. The free radical scavenging activity of tetrandrine is responsible for its inhibition of PMA-**induced** NF-kappaB activation.

L14 ANSWER 4 OF 60 MEDLINE

ACCESSION NUMBER: 2000125795 MEDLINE

DOCUMENT NUMBER: 20125795

TITLE: Inhibitory effects of 1,3-diaminopropane, an ornithine decarboxylase inhibitor, on rat two-stage urinary bladder carcinogenesis initiated by N-butyl-N-(4-hydroxybutyl)nitrosamine.

AUTHOR: Salim E I; Wanibuchi H; Morimura K; Kim S; Yano Y; Yamamoto

S; Fukushima S
 CORPORATE SOURCE: First Department of Pathology, Department of Pharmacology and Second Department of Biochemistry, Osaka City University Medical School, 1-4-3 Asahi-machi, Abeno-Ku, Osaka 545-8585, Japan.

SOURCE: CARCINOGENESIS, (2000 Feb) 21 (2) 195-203.

Journal code: C9T. ISSN: 0143-3334.

PUB. COUNTRY: ENGLAND: United Kingdom
 Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 200006

ENTRY WEEK: 20000602

AB Overexpression of ornithine decarboxylase (ODC) has been shown to be characteristic of tumor development and progression in humans and experimental animals. Therefore, we have examined the effects of 1,3-diaminopropane dihydrochloride (DAP), a potent inhibitor of ODC, on rat two-stage urinary bladder carcinogenesis initiated with

N-butyl-N-(4-hydroxybutyl)nitrosamine (BBN). In experiment 1 (36 weeks), 6-week-old F344 male rats were administered 0.05% BBN in drinking water for 4 weeks and then divided into four groups. Animals of groups 1 and 2 received basal diet and drinking water supplemented with or without DAP

(2

g/l). Groups 3 and 4 were given diet containing 5% sodium L-**ascorbate** (NaAsA), a typical urinary bladder tumor **promoter**, and drinking water with or without DAP. Administration of DAP to group 1 significantly reduced tumor size, multiplicity and incidence, particularly of papillomas, when compared with group 2 values. DAP together with NaAsA (group 3) also decreased tumor size relative to the group 4 case. To determine the effects of DAP on the early stages of bladder carcinogenesis and its mechanisms, a similar protocol was conducted (experiment 2) with death after 20 weeks. DAP treatment caused complete inhibition (0% incidence) of papillary and/or nodular

hyperplasia

in group 1 but was without influence in group 3, as compared with the respective controls. Moreover, the ODC activity, bromodeoxyuridine labeling indices and mRNA expression levels of cyclin D1 in the urinary bladder mucosa, determined by northern blotting, were markedly lower in group 1 than in group 2, but values were comparable for both groups administered NaAsA. Assessment of mRNA expression levels of the

angiogenic

vascular endothelial growth factor suggested no involvement in the inhibitory effects of DAP on urinary bladder carcinogenesis. The results indicate that inhibition of ODC could reduce urinary bladder carcinogenesis in rats, particularly in the early stages, through antiproliferative mechanisms.

L14 ANSWER 5 OF 60 MEDLINE

ACCESSION NUMBER: 2000120404 MEDLINE

DOCUMENT NUMBER: 20120404

TITLE: Concentration dependent promoting effects of sodium L-ascorbate with the same total dose in a rat two-stage urinary bladder carcinogenesis.

AUTHOR: Chen T X; Wanibuchi H; Wei M; Morimura K; Yamamoto S; Hayashi S; Fukushima S

CORPORATE SOURCE: Department of Pathology, Osaka City University Medical School, Osaka, Japan.. fukuchan@med.osaka-cu.ac.jp

SOURCE: CANCER LETTERS, (1999 Nov 1) 146 (1) 67-71.

Journal code: CMX. ISSN: 0304-3835.

PUB. COUNTRY: Ireland

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 200004

ENTRY WEEK: 20000403

AB Sodium L-**ascorbate** (Na-AsA) has been demonstrated to be a strong **promoter** of rat urinary bladder tumor development initiated by N-butyl-N-(4-hydroxybutyl)nitrosamine (BBN). In the present study, we investigated variation in its promoting activity when the same total dose was given with different concentrations and exposure times. After 4 weeks administration of 0.05% BBN, group 1 served as a control without any post-initiation treatment. The rats in groups 2-4 received 1.25% Na-AsA diet for 36 weeks, 2.5% Na-AsA for 18 weeks and 5% Na-AsA for 8 weeks, respectively. Tumor number (papillomas and carcinomas) was greatest in group 3, and area in group 4 ($P < 0.05$). However, no enhancement was

noted

in group 2, although preneoplastic lesions were significantly increased. These results suggest that with the same total administration dose, high concentration of Na-AsA has the strongest promoting effects on tumor development in urinary bladder carcinogenesis.

L14 ANSWER 6 OF 60 MEDLINE

ACCESSION NUMBER: 2000058358 MEDLINE

DOCUMENT NUMBER: 20058358

TITLE: Direct observation of stress response in Caenorhabditis elegans using a reporter transgene.
 AUTHOR: Link C D; Cypser J R; Johnson C J; Johnson T E
 CORPORATE SOURCE: Institute for Behavioral Genetics, University of Colorado Boulder 80309-0447, USA.. linkc@colorado.edu
 CONTRACT NUMBER: AG12423 (NIA)
 PO1-AG08761 (NIA)
 KO2-AA00195 (NIAAA)
 +
 SOURCE: CELL STRESS AND CHAPERONES, (1999 Dec) 4 (4) 235-42.
 Journal code: CV5. ISSN: 1355-8145.
 PUB. COUNTRY: United States
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200002
 ENTRY WEEK: 20000204

AB Transgenic Caenorhabditis elegans expressing jellyfish Green Fluorescent Protein under the control of the **promoter** for the **inducible** small heat shock protein gene hsp-16-2 have been constructed. Transgene expression parallels that of the endogenous hsp-16 gene, and, therefore, allows direct visualization, localization, and quantitation of hsp-16 expression in living animals. In addition to the expected upregulation by heat shock, we show that a variety of stresses, including exposure to superoxide-generating redox-cycling quinones and the expression of the human beta amyloid peptide, specifically **induce** the reporter transgene. The quinone **induction** is suppressed by coincubation with L-**ascorbate**. The ability to directly observe the stress response in living animals significantly simplifies the identification of both exogenous treatments and genetic alterations that modulate stress response, and possibly life span, in C. elegans.

L14 ANSWER 7 OF 60 MEDLINE

ACCESSION NUMBER: 2000008589 MEDLINE
 DOCUMENT NUMBER: 20008589
 TITLE: Loss of heterozygosity in (LewisxF344)F1 rat urinary bladder tumors **induced** with N-butyl-N-(4-hydroxybutyl)nitrosamine followed by dimethylarsinic acid or sodium L-ascorbate.
 AUTHOR: Chen T; Na Y; Wanibuchi H; Yamamoto S; Lee C C; Fukushima S
 CORPORATE SOURCE: Department of Pathology, Osaka City University Medical School, Osaka.
 SOURCE: JAPANESE JOURNAL OF CANCER RESEARCH, (1999 Aug) 90 (8) 818-23.
 Journal code: HBA. ISSN: 0910-5050.
 PUB. COUNTRY: Japan
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals; Cancer Journals
 ENTRY MONTH: 200001
 ENTRY WEEK: 20000104

AB Dimethylarsinic acid (DMA), a main metabolite of arsenicals which are carcinogenic in man, exerts tumor-promoting activity on rat urinary bladder carcinogenesis initiated with N-butyl-N-(4-hydroxybutyl)nitrosamine (BBN). Sodium L-**ascorbate** (Na-AsA) is also a strong tumor **promoter** in this animal model. In this study, we used (LewisxF344)F, rats to compare molecular alterations in urinary bladder tumors caused by BBN followed by DMA or Na-AsA. Male, 6-week-old rats were given 0.05% BBN in their drinking water for 4 weeks, and then the rats in group 1 were maintained with no further treatment for 40 weeks. The animals of groups 2 and 3 were administered 0.01% DMA in their drinking water (group 2) or 5% Na-AsA in the powder diet (group 3) after the BBN treatment. Group 4 rats were given 0.05% BBN continuously

for 36 weeks. At weeks 12, 20, 36 and 44, subgroups of rats were killed. Histopathological examination revealed promoting activity for DMA and, to a greater extent, Na-AsA on urinary bladder carcinogenesis. Loss of heterozygosity (LOH), detected with the polymerase chain reaction using

36

microsatellite markers, was found to be present in 2 of 9 (22%) urinary bladder tumors after treatment with DMA and 3 of 22 (14%) **induced** by continuous administration with BBN. No LOH was, however, detected in urinary bladder tumors after treatment with Na-AsA. The results thus suggest that the mechanisms of action of these two promoters, DMA and Na-AsA, may differ in rat urinary bladder carcinogenesis.

L14 ANSWER 8 OF 60 MEDLINE

ACCESSION NUMBER: 1999253748 MEDLINE

DOCUMENT NUMBER: 99253748

TITLE: Palmitoyl ascorbate: selective augmentation of procollagen mRNA expression compared with L-ascorbate in human intestinal smooth muscle cells.

AUTHOR: Rosenblat G; Willey A; Zhu Y N; Jonas A; Diegelmann R F; Neeman I; Graham M F

CORPORATE SOURCE: Department of Food Engineering and Biotechnology, Technion-Israel Institute of Technology, Haifa, Israel.

CONTRACT NUMBER: DK34151 (NIDDK)
GM20298 (NIGMS)

SOURCE: JOURNAL OF CELLULAR BIOCHEMISTRY, (1999 Jun 1) 73 (3) 312-20.

Journal code: HNF. ISSN: 0730-2312.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199910

ENTRY WEEK: 19991001

AB The effect of 6-O-palmitoyl **ascorbate** on procollagen mRNA levels, collagen synthesis, and collagen secretion was investigated and compared with the effect of L-**ascorbate** in human intestinal smooth muscle (HISM) cells in vitro. Collagen synthesis, determined by the

incorporation of 3H-proline into pepsin-resistant, salt-precipitated collagen, increased in a concentration-dependent manner in response to palmitoyl **ascorbate**. There was a twofold increase in collagen synthesis at 2.5 and 5 microM. By contrast, L-**ascorbate** was required at 4-5 times the concentration for the same response. However,

at

20 microM, both palmitoyl and L-**ascorbate** induced similar 2.7-fold increases in collagen synthesis. Palmitoyl **ascorbate** induced a 1.6- and 3.5-fold increase in steady-state levels of procollagen I and III mRNA levels respectively, whereas L-**ascorbate** had no effect. Palmitoyl **ascorbate** and L-**ascorbate** induced similar increases in the amounts of newly synthesized procollagen secreted into the medium and in the amounts of collagen types I, III and V accumulating in the cell

layer.

There was no effect of either palmitoyl **ascorbate** or L-**ascorbate** on the activity of a procollagen alpha2 (I) **promoter** construct transiently transfected into HISM cells. Palmitoyl **ascorbate** augments HISM cell procollagen synthesis and mRNA levels more efficiently than L-**ascorbate**. This property may be due to the greater resistance of the **ascorbate** ester to oxidation and suggests that palmitoyl **ascorbate** could be an important agent for studies of collagen synthesis in vitro.

L14 ANSWER 9 OF 60 MEDLINE

ACCESSION NUMBER: 1999026302 MEDLINE

DOCUMENT NUMBER: 99026302

TITLE: The heat-shock element is a functional component of the

Arabidopsis APX1 gene promoter.
 AUTHOR: Storozhenko S; De Pauw P; Van Montagu M; Inze D; Kushnir S
 CORPORATE SOURCE: Laboratorium voor Genetica, Departement Genetica, Vlaams
 Interuniversitair Instituut voor Biotechnologie, Belgium.
 SOURCE: PLANT PHYSIOLOGY, (1998 Nov) 118 (3) 1005-14.
 Journal code: P98. ISSN: 0032-0889.
 PUB. COUNTRY: United States
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199903
 ENTRY WEEK: 19990303

AB **Ascorbate** peroxidases are important enzymes that detoxify hydrogen peroxide within the cytosol and chloroplasts of plant cells. To better understand their role in oxidative stress tolerance, the transcriptional regulation of the apx1 gene from Arabidopsis was studied. The apx1 gene was expressed in all tested organs of Arabidopsis; mRNA levels were low in roots, leaves, and stems and high in flowers. Steady-state mRNA levels in leaves or cell suspensions increased after treatment with methyl viologen, ethephon, high temperature, and illumination of etiolated seedlings. A putative heat-shock cis element found in the apx1 **promoter** was shown to be recognized by the tomato (Lycopersicon esculentum) heat-shock factor in vitro and to be responsible for the in vivo heat-shock **induction** of the gene. The heat-shock cis element also contributed partially to the **induction** of the gene by oxidative stress. By using in vivo dimethyl sulfate footprinting, we showed that proteins interacted with a G/C-rich element found in the apx1 **promoter**.

L14 ANSWER 10 OF 60 MEDLINE

ACCESSION NUMBER: 1998340217 MEDLINE
 DOCUMENT NUMBER: 98340217

TITLE: Evaluation of a spectrophotometric assay for the measurement of malondialdehyde and 4-hydroxyalkenals in human spermatozoa: relationships with semen quality and sperm function.

AUTHOR: Gomez E; Irvine D S; Aitken R J
 CORPORATE SOURCE: MRC Reproductive Biology Unit, Edinburgh, UK.
 SOURCE: INTERNATIONAL JOURNAL OF ANDROLOGY, (1998 Apr) 21 (2) 81-94.

Journal code: GQK. ISSN: 0105-6263.
 PUB. COUNTRY: ENGLAND: United Kingdom
 Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199811
 ENTRY WEEK: 19981104

AB A spectrophotometric assay for the measurement of malondialdehyde and 4 hydroxyalkenals (MA + 4HA) has been evaluated for the detection of sperm pathologies involving oxidative stress. In order to make sensitive measurements of MA + 4HA on human spermatozoa, the stimulation of a lipid peroxidation cascade with a ferrous ion **promoter** was found to be necessary. The optimal configuration for the **promoter** was defined (0.64 mM FeSO4 + 20 mM **ascorbate** for 2 h in Ca2+ and Mg2 free Hanks' balanced salt solution) and the assay used in a series of studies to elucidate the functional significance of MA + 4HA determinations. Such measurements were found to give highly significant correlations (p < 0.001) with the loss of motility **induced** by oxidative stress created either with a xanthine oxidase, free radical generating system or by prolonged incubation under aerobic conditions. Experiments involving the stimulation and suppression of lipid peroxide release from human sperm suspensions, in concert with a bioassay for cytotoxicity, confirmed the strength and causative nature of these associations. Measurements of lipid peroxidation potential in highly purified, leucocyte-free sperm suspensions revealed the presence of inverse correlations with the motility of the spermatozoa, their

viability, their competence for sperm-oocyte fusion and, most significantly, the quality of sperm movement in the original semen samples. Similar negative correlations were observed between sperm function and phorbol ester-stimulated reactive oxygen species generation but, unlike the MA + 4HA determinations, these relationships were obfuscated by the presence of leucocytes. We conclude that the measurement of MA + 4HA in human spermatozoa provides important information on the underlying quality of spermatogenesis and should be of value in the clinical diagnosis of infertility involving oxidative stress and the selection of patients for antioxidant therapy.

=> d 114 ibib abs 11-20

L14 ANSWER 11 OF 60 MEDLINE
ACCESSION NUMBER: 1998333806 MEDLINE
DOCUMENT NUMBER: 98333806
TITLE: White blood cells cause oxidative damage to the fatty acid composition of phospholipids of human spermatozoa.
AUTHOR: Zalata A A; Christophe A B; Depuydt C E; Schoonjans F; Comhaire F H
CORPORATE SOURCE: University Hospital Ghent, Department of Internal Medicine, Belgium.
SOURCE: INTERNATIONAL JOURNAL OF ANDROLOGY, (1998 Jun) 21 (3) 154-62.
Journal code: GQK. ISSN: 0105-6263.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY WEEK: 19981103
AB The lipid composition of the sperm membrane has been shown to exert a significant effect upon the functional quality of spermatozoa. We have studied the effect of **induced** peroxidation and of the presence of polymorphonuclear white blood cells (WBCs) on the fatty acid composition of the phospholipids of human spermatozoa. The spermatozoa were fractionated by a discontinuous Percoll gradient in two fractions (47% and 90% Percoll). **Induced** peroxidation of spermatozoa was assessed by determining the production of thiobarbituric acid reactive substances (TBARS), mostly malondialdehyde, after incubation with ferrous sulphate and sodium **ascorbate** as a **promoter** of peroxidation. TBARS production after **induction** of peroxidation was correlated with the abundance of polyunsaturated fatty acids (PUFA) ($r = 0.68$, $p < 0.0001$), with the double bond index ($r = 0.72$, $p < 0.0001$), and with the oxidative potential index ($r = 0.73$, $p < 0.0001$) of fatty acids of phospholipids. In comparison with samples containing $> 1 \times 10^6$ WBCs/mL, those with $< 1 \times 10^6$ WBCs/mL contained higher proportions of PUFA (90% Percoll, $p < 0.05$; 47% Percoll, $p < 0.05$), total omega 3 fatty acids (90% Percoll, $p < 0.05$; 47% Percoll, $p < 0.001$), docosahexaenoic acid (90% Percoll $p < 0.05$; 47% Percoll, $p < 0.05$), and double bond index (90% Percoll, $p < 0.05$; 47% Percoll, $p < 0.001$). In addition, mean melting point was significantly lower (90% Percoll, $p < 0.05$; 47% Percoll, $p < 0.001$) in samples with $< 1 \times 10^6$ WBCs, indicating higher membrane fluidity. The increase of TBARS production by spermatozoa after incubation with the xanthine-xanthine oxidase system and/or ferrous sulphate as **promoter** of peroxidation was associated with a significant decrease of PUFA. Incubation of spermatozoa with WBCs, with or without activation by phorbol ester, decreased the PUFA ($p < 0.05$). Also, TBARS production was increased ($p < 0.01$) after activation of WBCs with phorbol ester. Our data provide evidence that oxidative stress **induced**

by WBCs has a damaging effect on the polyunsaturated fatty acids of sperm phospholipids which may result, amongst other effects, in decreased membrane fluidity.

L14 ANSWER 12 OF 60 MEDLINE

ACCESSION NUMBER: 97455923 MEDLINE

DOCUMENT NUMBER: 97455923

TITLE: Quantitative trait loci associated with promoting effects of sodium L-ascorbate on two-stage bladder carcinogenesis in rats.

AUTHOR: Kamoto T; Mori S; Murai T; Yamada Y; Makino S; Yoshida O; Hiai H

CORPORATE SOURCE: Department of Pathology and Biology of Diseases, Graduate School of Medicine, Kyoto University.

SOURCE: JAPANESE JOURNAL OF CANCER RESEARCH, (1997 Jul) 88 (7) 633-8.

Journal code: HBA. ISSN: 0910-5050.

PUB. COUNTRY: Japan

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199712

ENTRY WEEK: 19971204

AB In the two-stage rat bladder carcinogenesis model using N-butyl-N-(4-hydroxybutyl)nitrosamine (BBN) as an initiator and sodium L-ascorbate (SA) as a **promoter**, we found a notable strain difference between F344/DuCrj (F344) and WS/Shi (WS) rats in susceptibility to the promoting effect of SA. Twenty each of F344, WS and reciprocal F1 hybrid rats were given 0.05% BBN in their drinking water

for

a 4 weeks and then a basal diet with (BBN-SA group) or without (BBN group)

5% SA supplement for 32 weeks. In F344 and also in reciprocal F1 hybrids, the number of tumors per rat was significantly higher in the BBN-SA group than in the BBN group ($P < 0.0001$). In contrast, WS rats were not significantly affected by either treatment ($P = 0.8$). These findings indicate that F344 rats are highly susceptible to the **promoter** effect of SA, but WS rats are not. Linkage analysis of 108 WSx (WS x F344)

F1 backcrosses revealed that this difference was related to a quantitative

trait locus mapped on rat Chr. 17 (maximum LOD score, 3.86) named Bladder Tumor Susceptible-1 and possibly another locus on Chr. 5 (maximum LOD score, 2.39). This study has provided the first evidence that host genes influence the risk of bladder cancer development.

L14 ANSWER 13 OF 60 MEDLINE

ACCESSION NUMBER: 97427281 MEDLINE

DOCUMENT NUMBER: 97427281

TITLE: Effects of iron chelates on the transferrin-free culture of

rat dermal fibroblasts through active oxygen generation.

AUTHOR: Yabe N; Matsui H

CORPORATE SOURCE: Department of Hygiene, Dokkyo University School of Medicine, Tochigi, Japan.

SOURCE: IN VITRO CELLULAR AND DEVELOPMENTAL BIOLOGY. ANIMAL, (1997 Jul-Aug) 33 (7) 527-35.

Journal code: BZE. ISSN: 1071-2690.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199801

ENTRY WEEK: 19980104

AB Effects of nonchelating and chelating agents at 10 mM on the serum-free culture of rat dermal fibroblasts were investigated. A strong

iron-chelating agent, iminodiacetic acid (IDA), and a weak one, dihydroxyethylglycine (DHEG), decreased iron permeation into preconfluent fibroblasts. A weak iron-chelating agent, glycylglycine (GG), a nonchelating agent, N-2-hydroxyethylpiperazine-N'-2-ethanesulfonic acid (HEPES), and human apotransferrin (10 micrograms/ml) increased the permeation with time. Iron may be essential for survival of fibroblasts because subconfluent fibroblasts exposed to 100 microM FeSO4 in combination with transferrin, HEPES, or GG significantly decreased to release lactate dehydrogenase into the medium. Superoxide dismutase and dimethyl sulfoxide blocked the enzyme release, suggesting that superoxide and hydroxyl radical **induce** cellular damage but hydrogen peroxide (H2O2) generated by superoxide dismutation does not. GG significantly reduced H2O2 cytotoxicity. DHEG acted as a potent **promoter** of the iron-stimulated cellular damage if **ascorbate** or H2O2 was added to the medium. FeSO4 and FeCl3 (50 to 100 microM) individually combined with IDA maximally promoted fibroblast proliferation. **Ascorbate** increased formation of thiobarbituric acid-reactive substances from deoxyribose in the medium supplemented with FeSO4 and either IDA or DHEG. Conversely, **ascorbate** decreased the formation in the medium with FeSO4 and with or without other agents. Fibroblast proliferation may thus be stimulated through the active oxygen generation mediated by a redox-cycling between Fe3+ and Fe2+, which are dissolved in the medium at a high concentration, rather than through delivery of iron into the cells.

L14 ANSWER 14 OF 60 MEDLINE

ACCESSION NUMBER: 97354114 MEDLINE

DOCUMENT NUMBER: 97354114

TITLE: Cloning of the pumpkin ascorbate oxidase gene and analysis of a cis-acting region involved in **induction** by auxin.

AUTHOR: Kisu Y; Harada Y; Goto M; Esaka M

CORPORATE SOURCE: Faculty of Applied Biological Science, Hiroshima University, Higashi-Hiroshima, Japan.

SOURCE: PLANT AND CELL PHYSIOLOGY, (1997 May) 38 (5) 631-7.
Journal code: BIG. ISSN: 0032-0781.

PUB. COUNTRY: Japan

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-D55677

ENTRY MONTH: 199710

ENTRY WEEK: 19971003

AB A genomic clone encoding **ascorbate** oxidase was isolated from pumpkin (Cucurbita sp.). This gene is consisted of four exons and three introns. Analyses of the **promoter** fusion to beta-glucuronidase reporter gene by transient expression assay in pumpkin fruit tissues suggested the existence of a cis-acting region responsible for auxin regulation.

L14 ANSWER 15 OF 60 MEDLINE

ACCESSION NUMBER: 97344237 MEDLINE

DOCUMENT NUMBER: 97344237

TITLE: Role of ascorbate in the activation of NF-kappaB by tumour necrosis factor-alpha in T-cells.

AUTHOR: Munoz E; Blazquez M V; Ortiz C; Gomez-Diaz C; Navas P

CORPORATE SOURCE: Departamento de Fisiologia e Inmunologia, Facultad de Medicina, Universidad de Cordoba, Avda. Menendez Pidal
s/n,

14071 Cordoba, Spain.

SOURCE: BIOCHEMICAL JOURNAL, (1997 Jul 1) 325 (Pt 1) 23-8.
Journal code: 9YO. ISSN: 0264-6021.

PUB. COUNTRY: ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199710
ENTRY WEEK: 19971002

AB The first product of **ascorbate** oxidation, the **ascorbate** free radical (AFR), acts in biological systems mainly as an oxidant, and through its role in the plasma membrane redox system exerts different effects on the cell. We have investigated the role of **ascorbate**, AFR and dehydroascorbate (DHA) in the activation of the NF-kappaB transcription factor in Jurkat T-cells stimulated by tumour necrosis factor-alpha (TNF-alpha). Here we show, by electrophoretic mobility shift assays, that **ascorbate** increases the binding of NF-kappaB to DNA in TNF-alpha-stimulated Jurkat cells. The ability of **ascorbate** to enhance cytoplasmic inhibitory Ikbalpha protein degradation correlates completely with its capacity to **induce** NF-kappaB binding to DNA and to potentiate NF-kappaB-mediated transactivation of the HIV-1 long terminal repeat **promoter** in TNF-alpha-stimulated Jurkat cells but not in cells stimulated with PMA plus ionomycin. AFR behaves like **ascorbate**, while DHA and **ascorbate** phosphate do not affect TNF-alpha-mediated NF-kappaB activation. These results provide new evidence for a possible relationship between the activation of the electron-transport system at the plasma membrane by **ascorbate** or its free radical and redox-dependent gene transcription in T-cells.

L14 ANSWER 16 OF 60 MEDLINE

ACCESSION NUMBER: 97186415 MEDLINE
DOCUMENT NUMBER: 97186415
TITLE: NF-kappa B-independent suppression of HIV expression by ascorbic acid.
AUTHOR: Harakeh S; Jariwalla R J
CORPORATE SOURCE: Linus Pauling Institute of Science and Medicine, Palo Alto, California 94306, USA.
SOURCE: AIDS RESEARCH AND HUMAN RETROVIRUSES, (1997 Feb 10) 13 (3) 235-9.
Journal code: ART. ISSN: 0889-2229.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY WEEK: 19970604

AB Ascorbic acid (**ascorbate** or vitamin C) has been shown to suppress the **induction** of HIV in latently infected T lymphocytic cells following stimulation with a tumor **promoter** (PMA) and inflammatory cytokine (TNF-alpha). To assess whether this inhibition was mediated via modulation of the cellular transcription factor, NF-kappa B, we carried out gel shift analysis on nuclear extracts prepared under different conditions of cell stimulation in the presence or absence of **ascorbate**, N-acetylcysteine (NAC), or zidovudine (AZT). Pretreatment of ACH-2 T cells by NAC followed by stimulation with PMA, TNF-alpha, or hydrogen peroxide (H2O2) resulted in strong suppression of NF-kappa B activation. In contrast, neither **ascorbate** nor AZT affected NF-kappa B activity under all three **induction** conditions in the ACH-2 cell line. **Ascorbate** and AZT also had no effect on NF-kappa B activation following TNF-alpha- or PMA-**induced** stimulation of U1 promonocytic cells. These results suggest that the molecular mechanism of HIV inhibition by **ascorbate** is not mediated via NF-kappa B inhibition, unlike that seen with other antioxidants.

L14 ANSWER 17 OF 60 MEDLINE

ACCESSION NUMBER: 97181023 MEDLINE
DOCUMENT NUMBER: 97181023
TITLE: A hot spot for hydrogen peroxide-**induced** damage in the human hypoxia-**inducible** factor 1 binding site of the PGK 1 gene.
AUTHOR: Rodriguez H; Drouin R; Holmquist G P; Akman S A

CORPORATE SOURCE: Beckman Research Institute, City of Hope National Medical Center, Duarte, California, 91010, USA.
CONTRACT NUMBER: CA53115 (NCI)
SOURCE: ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, (1997 Feb 15) 338 (2) 207-12.
Journal code: 6SK. ISSN: 0003-9861.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199705
ENTRY WEEK: 19970503

AB Using ligation-mediated polymerase chain reaction to separately map the distribution of **induced** oxidized bases and strand breaks along the human PGK1 **promoter** at nucleotide resolution, we previously described the pattern of oxidative DNA damage **induced** in vitro by Cu(II)/**ascorbate**/H₂O₂ [J. Biol. Chem. 270, 17633-17640 (1995)]. Here we report that the pattern of in vivo base damage caused by H₂O₂ is almost identical to that of the previously used in vitro system with the exception of transcription factor-associated footprints. An unusually strong positive footprint for both strand breaks and oxidized bases is associated with binding of the hypoxia-**inducible** transcription factor-1. Base damage at this footprint was 52-91% repaired in 24 h, which was similar to the global base damage repair rate.

However,
strand breaks at this footprint were only 39-55% repaired in 24 h or approximately 100-fold slower than the global strand break repair rate.

L14 ANSWER 18 OF 60 MEDLINE

ACCESSION NUMBER: 96281685 MEDLINE
DOCUMENT NUMBER: 96281685
TITLE: Antioxidants inhibit the enhancement of malignant cell transformation **induced** by 2,3,7,8-tetrachlorodibenzo-p-dioxin.
AUTHOR: Wolffe D; Marquardt H
CORPORATE SOURCE: Department of Toxicology, University of Hamburg Medical School, Germany.
SOURCE: CARCINOGENESIS, (1996 Jun) 17 (6) 1273-8.
Journal code: C9T. ISSN: 0143-3334.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199610

AB The mechanisms of the tumor promoting activity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) were studied using as in vitro model the enhancement ('promotion') of malignant transformation of C3H/M2 mouse fibroblasts **induced** by N-methyl-N'-nitro-N-nitrosoguanidine or 3-methylcholanthrene. In this assay, the promoting effect of TCDD was maximal at a very low concentration of 1.5 pM and was comparable to the effect of the reference tumor **promoter**, 12-O-tetradecanoylphorbol-13-acetate (TPA, 0.25 microg/ml). The role of reactive oxygen species in the promoting action was investigated: mannitol, a scavenger of hydroxyl radicals, or antioxidants, i.e.

ascorbic

acid plus alpha-tocopherol, abolished the in vitro promoting effects of TPA and TCDD. Furthermore, the involvement of protein kinase C (PKC) activation was studied: the protein kinase inhibitor H-7 markedly reduced the in vitro promoting activity of TPA but did not affect the promotion

by

TCDD. In accord with these results, TPA, but not TCDD, enhanced the PKC activity in C3H/M2 fibroblasts. Since the TPA-mediated activation of PKC was not affected by **ascorbate** plus alpha-tocopherol, it is concluded that the antioxidants interfere with tumor promotion at a step beyond PKC activation. Thus, the results suggest that the enhancement of malignant cell transformation by TPA and TCDD is dependent on a common

mechanism, possibly **induced** by oxygen radicals, and, in addition, on further mechanisms that may involve agent-specific signalling pathways (e.g. PKC activation by TPA).

L14 ANSWER 19 OF 60 MEDLINE

ACCESSION NUMBER: 96066714 MEDLINE

DOCUMENT NUMBER: 96066714

TITLE: Activation of hepatic stellate cells by TGF alpha and collagen type I is mediated by oxidative stress through c-myb expression.

AUTHOR: Lee K S; Buck M; Houglum K; Chojkier M

CORPORATE SOURCE: Department of Medicine, Veterans Affairs Medical Center, San Diego, California, USA.

CONTRACT NUMBER: DK-38652 (NIDDK)

DK-46971 (NIDDK)

GM-47165 (NIGMS)

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SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (1995 Nov) 96 (5) 2461-8.

Journal code: HS7. ISSN: 0021-9738.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals

ENTRY MONTH: 199602

AB Excessive production of collagen type I is a major contributor to hepatic fibrosis. Activated (myofibroblastic), but not quiescent, hepatic stellate

cells (lipocytes) have a high level of collagen type I and alpha-smooth muscle actin expression. Therefore, stellate cell activation is a critical

step in hepatic fibrosis. Here we show that quiescent stellate cells were activated by the generation of free radicals with **ascorbate** /FeSO4 and by malondialdehyde, a product of lipid peroxidation. In addition, stellate cell activation by collagen type I matrix and TGF

alpha

was blocked by antioxidants, such as d-alpha-tocopherol and butylated hydroxytoluene. Moreover, oxidative stress, TGF alpha and collagen type I markedly stimulated stellate cell entry into S-phase, NFkB activity, and c-myb expression, which were prevented by antioxidants. c-myb antisense oligonucleotide blocked the activation and proliferation of stellate

cells

induced by TGF alpha. Nuclear extracts from activated, but not from quiescent, stellate cells formed a complex with the critical **promoter** E box of the alpha-smooth muscle actin gene, which was disrupted by c-myb and NFkB65 antibodies, and competed by c-myb and NFkB cognate DNA. c-Myb expression was also stimulated in activated stellate cells in carbon tetrachloride-**induced** hepatic injury and fibrogenesis. This study indicates that oxidative stress plays an essential role, through the **induction** of c-myb and NFkB, on stellate cell activation.

L14 ANSWER 20 OF 60 MEDLINE

ACCESSION NUMBER: 95394900 MEDLINE

DOCUMENT NUMBER: 95394900

TITLE: Molecular cloning and heterologous expression of the gene encoding dihydrogeodin oxidase, a multicopper blue enzyme from *Aspergillus terreus*.

AUTHOR: Huang K X; Fujii I; Ebizuka Y; Gomi K; Sankawa U

CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, University of Tokyo, Japan.

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Sep 15) 270 (37) 21495-502.

Journal code: HIV. ISSN: 0021-9258.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-D49538
ENTRY MONTH: 199512

AB Aspergillus terreus dihydrogeodin oxidase (DHGO) is an enzyme catalyzing the stereospecific phenol oxidative coupling reaction converting dihydrogeodin to (+)-geodin. We previously reported the purification of DHGO from A. terreus and raised polyclonal antibody against DHGO. From the

first cDNA library constructed in lambda gt11 using mRNA from 3-day-old mycelium of A. terreus, four clones were identified using anti-DHGO antibody, but all contained partial cDNA inserts around 280 base pairs. This cDNA fragment was used as a probe to clone the genomic DNA and cDNA for dihydrogeodin oxidase from A. terreus. The sequence of the cloned

DHGO genomic DNA and cDNA predicted that the DHGO polypeptide consists of 605 amino acids showing significant homology with multicopper blue proteins such as laccase and **ascorbate** oxidase. Four potential copper binding domains exist in DHGO polypeptide. The DHGO gene consists of seven

exons separated by six short introns. Expression of the DHGO gene in Aspergillus nidulans under the starch or maltose-inducible Taka-amylase A promoter as an active enzyme established the functional identity of the gene. Also, introduction of the genomic DNA

for DHGO into Penicillium frequentans led to the production of DHGO polypeptide as judged by Western blot analysis.

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L14 ANSWER 21 OF 60 MEDLINE

ACCESSION NUMBER: 95340566 MEDLINE

DOCUMENT NUMBER: 95340566

TITLE: Mapping of copper/hydrogen peroxide-induced DNA damage at nucleotide resolution in human genomic DNA by ligation-mediated polymerase chain reaction.

AUTHOR: Rodriguez H; Drouin R; Holmquist G P; O'Connor T R; Boiteux

S; Laval J; Doroshow J H; Akman S A
CORPORATE SOURCE: Department of Medical Oncology and Therapeutics Research, City of Hope National Medical Center, Duarte, California 91010, USA.

CONTRACT NUMBER: CA-53115 (NCI)

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Jul 21) 270 (29) 17633-40.

Journal code: HIV. ISSN: 0021-9258.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Cancer Journals; Priority Journals

ENTRY MONTH: 199510

AB The ligation-mediated polymerase chain reaction was used to map the frequency of reactive oxygen species-induced DNA damage at nucleotide resolution in genomic DNA purified from cultured human male fibroblasts. Damaged pyrimidine and purine bases were recognized and cleaved by the Nth and Fpg proteins from Escherichia coli, respectively. Strand breaks and modified bases were induced in vitro by copper ion-mediated reduction of hydrogen peroxide in the presence of **ascorbate**; reactant concentrations were adjusted to induce lesions at a frequency of 1 per 2-3 kilobases in purified genomic DNA. Glyoxal gel analysis demonstrated that the ratio of induced strand breaks to induced base damage was 0.8/2.7 in DNA dialyzed

extensively to remove adventitious transition metal ions. Ligation-mediated polymerase chain reaction analysis of the damage frequency in the **promoter** region of the transcriptionally active phosphoglycerate kinase (PGK 1) gene revealed that (Cu(II)/**ascorbate**)/H₂O₂ caused DNA base damage by a sequence-dependent mechanism, with the 5' bases of d(pGn) and d(pCn) being damage hot spots, as were the most internal guanines of d(pGGGCCCC) and d(pCCCCGGG). Since base damage occurs after formation of a DNA-Cu(I)-H₂O₂ complex, these

data

suggest that the local DNA sequence affects formation of DNA-Cu(I)-H₂O₂ complexes and/or the efficiency of base oxidation during resolution of this complex.

L14 ANSWER 22 OF 60 MEDLINE

ACCESSION NUMBER: 94280430 MEDLINE

DOCUMENT NUMBER: 94280430

TITLE: Tamoxifen and hydroxytamoxifen as intramembraneous inhibitors of lipid peroxidation. Evidence for peroxy radical scavenging activity.

AUTHOR: Custodio J B; Dinis T C; Almeida L M; Madeira V M

CORPORATE SOURCE: Laboratorio de Bioquimica, Faculdade de Farmacia, Universidade de Coimbra, Portugal..

SOURCE: BIOCHEMICAL PHARMACOLOGY, (1994 Jun 1) 47 (11) 1989-98. Journal code: 9Z4. ISSN: 0006-2952.

PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199409

AB Tamoxifen (TAM) is the antiestrogen most widely used in the chemotherapy and chemoprevention of breast cancer. It has been reported that TAM and its more active metabolite 4-hydroxytamoxifen (OHTAM) **induce** multiple cellular effects, including antioxidant actions. Here sarcoplasmic reticulum membranes (SR) were used as a simple model of oxidation to clarify the antioxidant action type and mechanisms of these anticancer drugs on lipid peroxidation **induced** by Fe²⁺/**ascorbate** and peroxy radicals generated by the water-soluble 2,2'-azobis(2-amidinopropane)dihydrochloride (AAPH) and by the lipid-soluble 2,2'-azobis(2,4-dimethylvaleronitrile) (AMVN). Peroxidation was monitored by different assay systems, namely cis-parinaric acid (PnA) fluorescence quenching, production of thiobarbituric acid-reactive substances, polyunsaturated fatty acids (PUFA) degradation and oxygen consumption. TAM and OHTAM are efficient inhibitors of lipid peroxidation **induced** by Fe²⁺/**ascorbate** and strong intramembraneous scavengers of peroxy radicals generated either in the water or lipid phases by AAPH and AMVN, respectively. However, these drugs are not typical chain-breaking antioxidant compounds as compared with vitamin E. Additionally, their antioxidant effectiveness enhances the protective capacity of vitamin E against lipid peroxidation **induced** by AMVN. OHTAM is a more powerful intramembraneous inhibitor of lipid peroxidation as compared with TAM; this effectiveness not correlating

with

alterations on membrane fluidity may be due to the presence of a hydrogen-donating HO-group in the OHTAM molecule and its preferential location in the outer bilayer regions where it can donate the hydrogen atom to quench free radicals capable of initiating the membrane oxidative degradation. The stronger OHTAM intramembraneous scavenger capacity over TAM also correlates with its higher partition in biomembranes. Therefore, the strong peroxy radical scavenger activity of OHTAM in the hydrophobic membrane phase may putatively contribute to the mechanisms of cytostatic and chemopreventive action of its **promoter** TAM on development of breast cancer.

L14 ANSWER 23 OF 60 MEDLINE

ACCESSION NUMBER: 94105329 MEDLINE

DOCUMENT NUMBER: 94105329

TITLE: Apple ripening-related cDNA clone pAP4 confers ethylene-forming ability in transformed *Saccharomyces cerevisiae*.
AUTHOR: Wilson I D; Zhu Y; Burmeister D M; Dilley D R
CORPORATE SOURCE: Department of Horticulture, Michigan State University, East Lansing 48824.
SOURCE: PLANT PHYSIOLOGY, (1993 Jul) 102 (3) 783-8.
Journal code: P98. ISSN: 0032-0889.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199404

AB The apple ripening-related cDNA insert of clone pAP4 (G.S. Ross, M.L. Knighton, M. Lay-Yee [1992] Plant Mol Biol 19: 231-238) has previously been shown to have considerable nucleic acid and predicted amino acid sequence similarity to the insert of a tomato ripening-related cDNA clone (pTOM13) that is known to encode the enzyme 1-aminocyclopropane-1-carboxylate (ACC) oxidase (A.J. Hamilton, G.W. Lycett, D. Grierson [1990] Nature 346: 284-287; A.J. Hamilton, M. Bouzayen, D. Grierson [1991] Proc Natl Acad Sci USA 88: 7434-7437). The cDNA insert from the clone pAP4 was fused between the galactose-inducible promoter and the terminator of the yeast expression vector pYES2. Transformation of *Saccharomyces cerevisiae* strain F808- with this DNA construct and incubation of the yeast in the presence of D[+]-galactose allowed these cells to convert ACC to ethylene. The transformed yeast converted 1-amino-2-ethylcyclopropane-1-carboxylate isomers to 1-butene with the same 1R,2S-stereoselectivity as achieved by the native ACC oxidase from apples. Both **ascorbate** and Fe²⁺ ions stimulated the rate of the production of ethylene from ACC by the transformed yeast, whereas Cu²⁺

and

Co²⁺ were strongly inhibitory; these are features of ACC oxidase.

Northern

analysis of the total RNA from nontransformed and transformed yeast showed

that the ability to convert the ACC to ethylene was correlated with the synthesis and accumulation of a novel 1.2-kb mRNA that hybridized to the cDNA clone pAP4. We conclude that the cDNA sequence of the clone pAP4 encodes ACC oxidase.

L14 ANSWER 24 OF 60 MEDLINE

ACCESSION NUMBER: 94086149 MEDLINE

DOCUMENT NUMBER: 94086149

TITLE: **Induction** and promotion of forestomach tumors by sodium nitrite in combination with ascorbic acid or sodium ascorbate in rats with or without N-methyl-N'-nitro-N-nitrosoguanidine pre-treatment.

AUTHOR: Yoshida Y; Hirose M; Takaba K; Kimura J; Ito N

CORPORATE SOURCE: First Department of Pathology, Nagoya City University, Medical School, Japan..

SOURCE: INTERNATIONAL JOURNAL OF CANCER, (1994 Jan 2) 56 (1) 124-8.

Journal code: GQU. ISSN: 0020-7136.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199403

AB In experiment I, short-term effects of combined treatment with anti-oxidants, sodium **ascorbate** (NaAsA) and sodium nitrite (NaNO₂) on forestomach cell proliferation were examined in F344 male rats.

Groups of 5 animals aged 6 weeks were treated for 4 weeks with 0.8% catechol, 0.8% hydroquinone, 1% tert-butyl-hydroquinone (TBHQ), 2% gallic acid or 2% pyrogallol alone or in combination with 0.3% NaNO₂ in the

drinking water and/or 1% NaAsA in the diet. The thicknesses of forestomach mucosa in rats treated with anti-oxidants and NaNO₂ in combination were greater than those with antioxidant alone and additional NaAsA treatment further enhanced the thickening of mucosa. It was noteworthy that values for mucosae of animals treated with NaNO₂ and NaAsA without anti-oxidant were similar to those for anti-oxidants. In experiment 2, effects of combined treatment with NaAsA or ascorbic acid (AsA) and NaNO₂ on carcinogenesis were examined in F344 male rats with or without N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) pre-treatment. Groups of 20 or 15 rats, respectively, aged 6 weeks, were given a single intra-gastric administration of 150 mg/kg body weight of MNNG in DMSO:water = 1:1 or the vehicle alone by stomach tube. Starting 1 week later, they received supplements of 1% NaAsA or 1% AsA in the diet and 0.3% NaNO₂ in drinking water in combination, each of the individual chemicals alone, or basal diet until the end of week 52. In MNNG-treated animals, incidences of forestomach papillomas and carcinomas were significantly enhanced in the NaNO₂ alone group (84 and 47%, respectively) as compared with the basal diet group (30 and 10%), with further significant increase in carcinomas occurring with additional NaAsA (79%, p < 0.05) or AsA (85%, p < 0.05) treatment. In animals without MNNG, all animals in the NaNO₂ group demonstrated mild hyperplasia, additional administration of NaAsA or AsA remarkably enhancing the grade of hyperplasia, and resulting in 53% and 20% incidences, respectively, of papillomas. Thus NaNO₂ was demonstrated to exert **promoter** action for forestomach carcinogenesis, with NaAsA and AsA acting as co-promoters. The results strongly indicate that combined treatment with NaAsA or AsA and NaNO₂ may **induce** forestomach carcinomas in the long term.

L14 ANSWER 25 OF 60 MEDLINE

ACCESSION NUMBER: 93345640 MEDLINE

DOCUMENT NUMBER: 93345640

TITLE: Retinoic acid **induces** rapid mineralization and expression of mineralization-related genes in

chondrocytes.

AUTHOR: Iwamoto M; Shapiro I M; Yagami K; Boskey A L; Leboy P S; Adams S L; Pacifici M

CORPORATE SOURCE: Department of Anatomy-Histology, School of Dental Medicine,

University of Pennsylvania, Philadelphia 19104-6003..

CONTRACT NUMBER: AR 39705 (NIAMS)

AR 40833 (NIAMS)

AR 34411 (NIAMS)

+

SOURCE: EXPERIMENTAL CELL RESEARCH, (1993 Aug) 207 (2) 413-20.

Journal code: EPB. ISSN: 0014-4827.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199311

AB Numerous studies of experimental hypo- and hypervitaminosis A have long suggested that retinoic acid (RA) is involved in chondrocyte maturation during endochondral ossification and skeletogenesis. However, the specific

and direct roles of RA in these complex processes remain unclear. Based on

recent studies from our laboratories, we tested the hypothesis that RA **induces** the expression of genes associated with the terminal mineralization phase of chondrocyte maturation and promotes apatite deposition in the extracellular matrix. Cell populations containing chondrocytes at advanced stages of maturation were isolated from the

upper

portion of Day 18 chick embryo sterna and grown for 2 weeks in monolayer

until confluent. The cells were then treated with low doses (10-100 nM) of RA for up to 6 days in the presence of a phosphate donor (beta-glycerophosphate) but in the absence of ascorbic acid. Within 4 days of treatment, RA dramatically **induced** expression of the alkaline phosphatase (APase), osteonectin, and osteopontin genes, caused a several-fold increase in APase activity, and provoked massive mineral formation while it left type X collagen gene expression largely unchanged.

The mineral had a mean Ca/Pi molar ratio of 1.5; Fourier transform infrared spectra confirmed that it represented hydroxyapatite. Mineralization was completely abolished by treatment with parathyroid hormone; this profound effect confirmed that RA **induced** cell-mediated mineralization and not nonspecific precipitation. When cultures were treated with both RA and ascorbic acid, there was a slight further increase in APase activity and increased calcium accumulation.

The effects of RA were also studied in cultures of immature chondrocytes isolated from the caudal portion of sternum; however, RA only had minimal effects on mineralization and gene expression in these cells. Thus, RA appears to be a rapid, potent, maturation-dependent, **ascorbate**-independent **promoter** of terminal maturation and matrix calcification in chondrocytes.

L14 ANSWER 26 OF 60 MEDLINE

ACCESSION NUMBER: 92184667 MEDLINE

DOCUMENT NUMBER: 92184667

TITLE: The modifying effects of indomethacin or ascorbic acid on cell proliferation **induced** by different types of bladder tumor promoters in rat urinary bladder and forestomach mucosal epithelium.

AUTHOR: Shibata M A; Fukushima S; Asakawa E; Hirose M; Ito N

CORPORATE SOURCE: First Department of Pathology, Nagoya City University Medical School.

SOURCE: JAPANESE JOURNAL OF CANCER RESEARCH, (1992 Jan) 83 (1) 31-9.

Journal code: HBA. ISSN: 0910-5050.

PUB. COUNTRY: Japan

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199206

AB The effects of indomethacin (IM) or L-ascorbic acid (AsA) on cell proliferation **induced** by bladder tumor promoters such as butylated hydroxyanisole (BHA), sodium L-**ascorbate** (Na-AsA), sodium citrate (Na-Cit), and diphenyl (DP) in rat bladder and forestomach epithelium were investigated. Treatment with IM in combination with BHA

or

Na-AsA diminished DNA synthesis levels of bladder epithelium as compared to the BHA or Na-AsA alone values. On the other hand, AsA further amplified the increase of bladder epithelial DNA synthesis caused by Na-Cit treatment. Histopathologically, administration of Na-AsA in combination with IM reduced the incidence of simple hyperplasia. In contrast, simultaneous treatment with Na-Cit and AsA caused an increase

of

the hyperplasia development. No apparent combination effects were

observed

in the DP-treated groups. In forestomach epithelium, AsA enhanced the

BHA-

induced increase in DNA synthesis and epithelial hyperplasia, characterized by marked basal cell proliferation. The present results

thus

suggested that IM may exert inhibitory effects on promotion of bladder carcinogenesis by certain tumor **promoter** types, and AsA may enhance BHA forestomach carcinogenesis.

L14 ANSWER 27 OF 60 MEDLINE

ACCESSION NUMBER: 91165087 MEDLINE

DOCUMENT NUMBER: 91165087

TITLE: DNA synthesis and scanning electron microscopic lesions in renal pelvic epithelium of rats treated with bladder cancer

promoters.

AUTHOR: Shibata M A; Asakawa E; Hagiwara A; Kurata Y; Fukushima S

CORPORATE SOURCE: First Department of Pathology, Nagoya City University Medical School, Japan..

SOURCE: TOXICOLOGY LETTERS, (1991 Mar) 55 (3) 263-72.

Journal code: VXN. ISSN: 0378-4274.

PUB. COUNTRY: Netherlands

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199106

AB The proliferation response of rat renal pelvic epithelium, lined by transitional epithelium, to administration of various bladder cancer promoters was investigated. In addition, prostaglandin E2 (PGE2), lipid peroxide (LPO), malondialdehyde (MDA) and cyclic adenosine 3':5'-monophosphate (cyclic AMP) levels were assessed in urine of rats given the non-promoter L-ascorbic acid (AsA) and the promoters sodium L-ascorbate (AsA-Na) or sodium bicarbonate (NaHCO3) for 4 or 8 weeks. DNA synthesis in the renal pelvic epithelium, as assessed by 5-bromo-2'-deoxyuridine (BrdU) incorporation, was increased in the groups given AsA-Na, an extremely high dose of sodium chloride (NaCl), tert-butylhydroquinone (TBHQ) or ethoxyquin (EQ). Moreover, with the exception of AsA-Na, all treatments that induced an elevation of DNA synthesis also caused morphological epithelial alterations as observed

by scanning electron microscopy (SEM). Treatment with butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) did not result in any proliferative response of the rat renal pelvis. No treatment-related changes in urinary PGE2 and cyclic AMP were noted, although AsA-Na and

AsA

but not NaHCO3 reduced levels of LPO and MDA in the urine. The results indicate that while the response of renal pelvic epithelium to certain bladder cancer promoters is similar to that of the bladder itself, none

of

the urinary cellular growth or free radical biochemical parameters is directly related to urothelial cell proliferation.

L14 ANSWER 28 OF 60 MEDLINE

ACCESSION NUMBER: 90220639 MEDLINE

DOCUMENT NUMBER: 90220639

TITLE: Stable expression of full-length and truncated bovine peptidylglycine alpha-amidating monooxygenase

complementary

DNAs in cultured cells.

AUTHOR: Perkins S N; Eipper B A; Mains R E

CORPORATE SOURCE: Department of Neuroscience, Johns Hopkins University School

of Medicine, Baltimore, Maryland 21205.

CONTRACT NUMBER: DK-32948 (NIDDK)

DK-32949 (NIDDK)

DA-00097 (NIDA)

+

SOURCE: MOLECULAR ENDOCRINOLOGY, (1990 Jan) 4 (1) 132-9.

Journal code: NGZ. ISSN: 0888-8809.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199007

AB Peptidylglycine alpha-amidating monooxygenase (PAM; EC 1.14.17.3) catalyzes the production of alpha-amidated peptides from their glycine-extended precursors, a posttranslational modification often required for full biological activity. We have previously cloned cDNAs encoding a 108-kDa bovine PAM precursor. To confirm that this cDNA encodes a functional alpha-amidating enzyme and to begin to examine the structural requirements for the biosynthesis of an active PAM enzyme, we constructed expression vectors that placed the cDNA for either the full-sized enzyme or a form truncated at the carboxyl-terminal (and thus lacking the transmembrane domain) under the control of the mouse metallothionein-1 **promoter**. We used the resultant plasmids to transfect AtT-20 mouse anterior pituitary corticotrope cells and selected stable lines that expressed increased levels of PAM activity. Transfected cells in which expression from the metallothionein **promoter** had been **induced** had up to 15-fold higher levels of PAM mRNA and up to 7.5-fold higher levels of PAM activity than wild-type cells. The PAM activity in the transfected cells shared many enzymatic characteristics with PAM-B, a 38-kDa soluble form of PAM purified from bovine neurointermediate pituitary. These included copper- and **ascorbate**-dependent activity, an alkaline pH optimum for the peptide substrate D-Tyr-Val-Gly, similar affinities for several other synthetic substrates, and comparable apparent size during gel filtration. Compared to extracts of wild-type cells, extracts from transfected cells showed increased production of five different amino acid alpha-amides. These data indicate that a single enzyme can act on a variety of peptide substrates, and that the full structure of the PAM precursor is not necessary during biosynthesis for expression of active PAM enzyme.

L14 ANSWER 29 OF 60 MEDLINE

ACCESSION NUMBER: 89355227 MEDLINE

DOCUMENT NUMBER: 89355227

TITLE: Responses of rat urine and urothelium to bladder tumor promoters: possible roles of prostaglandin E2 and ascorbic acid synthesis in bladder carcinogenesis.

AUTHOR: Shibata M A; Yamada M; Asakawa E; Hagiwara A; Fukushima S

CORPORATE SOURCE: First Department of Pathology, Nagoya City University Medical School, Japan..

SOURCE: CARCINOGENESIS, (1989 Sep) 10 (9) 1651-6.

Journal code: C9T. ISSN: 0143-3334.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 198912

AB An investigation of sequential changes in urine composition, levels of DNA

synthesis and morphology of bladder epithelium following administration of

the tumor promoters sodium **ascorbate** (AsA-Na) or butylated hydroxyanisole (BHA) and the non-**promoter** ascorbic acid (AsA)

for 36 weeks was performed. In addition, prostaglandin E2 (PGE2), CAMP

and

AsA content were assessed in bladder tissue after 16 weeks. While AsA-Na caused increase in pH, sodium content and volume, and a decrease in osmolality of the urine throughout the study, these changes were not observed with AsA administration which resulted in a decrease in urinary pH. BHA treatment was not associated with any urinary changes. AsA-Na brought about a significant elevation of DNA synthesis in the bladder epithelium from weeks 2 to 16 and was associated with simple hyperplasia at week 8, which, however, decreased by week 16 and was no longer evident at weeks 24 and 36 when DNA synthesis returned to normal. Under the scanning electron microscope (SEM), morphologic alterations of the urothelial surface in rats given AsA-Na were observed at weeks 8 and 16, but the appearance at week 36 was almost normal. AsA did not cause any

changes in these parameters at any time point. BHA induced a significant elevation of DNA synthesis throughout the study, produced simple hyperplasia at week 36 and alterations of the epithelial surface from weeks 4 to 36. Significant increases of PGE2 and AsA in bladder tissue were noted for the AsA-Na or BHA, but not AsA groups. Moreover, cAMP levels in bladder tissue of rats exposed to AsA-Na or BHA were slightly higher than in the controls. The results suggest that changes in PGE2, cAMP and AsA may be involved in promotion of rat bladder carcinogenesis.

L14 ANSWER 30 OF 60 MEDLINE
ACCESSION NUMBER: 86085381 MEDLINE
DOCUMENT NUMBER: 86085381
TITLE: Correlation of results of agglutination assays with concanavalin A and carcinogenesis experiments on promoters of bladder cancer.
AUTHOR: Kakizoe T; Nishio Y; Ohtani M; Niijima T; Sato S; Sugimura T
SOURCE: JAPANESE JOURNAL OF CANCER RESEARCH, (1985 Oct) 76 (10) 930-6.
Journal code: HBA. ISSN: 0910-5050.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198604

AB The promoting effects of various chemicals and dietary constituents on bladder carcinogenesis were examined by means of a short-term assay, in which maintenance of concanavalin A agglutination of isolated rat bladder cells caused by a subcarcinogenic dose of N-butyl-N-(4-hydroxybutyl)nitrosamine was used as an indicator. Twenty-seven chemicals were examined as possible promoters. Positive results in this assay were consistent with established promoting effects in the cases of sodium saccharin, saccharin, sodium L-ascorbate, sodium cyclamate, DL-tryptophan, butylated hydroxyanisole, butylated hydroxytoluene, L-thioprolin and phenacetin. Allopurinol was the only established promoter that gave negative results in the agglutination assay. Thus, this method is useful for rapid evaluation of the specific promoting effect of a chemical on bladder carcinogenesis.

=> d history

(FILE 'HOME' ENTERED AT 15:14:04 ON 11 DEC 2000)

FILE 'MEDLINE, CAPLUS, LIFESCI, EMBASE, USPATFULL' ENTERED AT 15:14:47

ON

11 DEC 2000

L1 2 S ASCORBATE AND PROMOTER
L2 671 S ASCORBATE AND PROMOTER
L3 2 DUP REM L1 (0 DUPLICATES REMOVED)
L4 0 S L2 AND REPORTER
L5 45 S L2 AND REPORTER
L6 40 DUP REM L5 (5 DUPLICATES REMOVED)
L7 229 S ASCORBATE (P) PROMOTER
L8 7 S L7 (P) REPORTER
L9 2 DUP REM L8 (5 DUPLICATES REMOVED)
L10 8 S L7 AND REPORTER
L11 1 S L10 NOT L8
L12 189 S ASCORBATE (S) PROMOTER
L13 108 DUP REM L12 (81 DUPLICATES REMOVED)
L14 60 S L13 AND INDUC?

=> d l14 ibib abs 31-40

L14 ANSWER 31 OF 60 MEDLINE

ACCESSION NUMBER: 86003548 MEDLINE

DOCUMENT NUMBER: 86003548

TITLE: Carcinogenicity and modification of the carcinogenic response by BHA, BHT, and other antioxidants.

AUTHOR: Ito N; Fukushima S; Tsuda H

SOURCE: CRITICAL REVIEWS IN TOXICOLOGY, (1985) 15 (2) 109-50.

Ref:

187

Journal code: AFR. ISSN: 1040-8444.

PUB. COUNTRY:

United States

Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

198601

AB Carcinogenicity tests showed that addition of the antioxidant BHA to the diet of F344 rats **induced** high incidences of papilloma and squamous cell carcinoma of the forestomach of both sexes. Male hamsters given BHA for 24 weeks also developed papilloma showing downward growth into the submucosa of the forestomach. These results indicate that BHA should be classified in the category of "sufficient evidence of carcinogenicity" as judged by IARC criteria. The 3-tert isomer of BHA seemed to be responsible for the carcinogenicity of crude BHA in the forestomach of rats. BHT was not found to be carcinogenic in rats or mice.

In two-stage carcinogenesis in rats after appropriate initiation, BHA enhanced carcinogenesis in the forestomach and urinary bladder of rats, but inhibited carcinogenesis in the liver. BHT enhanced the **induction** of urinary bladder tumors and inhibited that of liver tumors, but had no effect on carcinogenesis in the forestomach. BHT could be a **promoter** of thyroid carcinogenesis. Sodium L-**ascorbate** enhanced forestomach and urinary bladder carcinogenesis. Ethoxyquin enhanced kidney and urinary bladder carcinogenesis, but inhibited liver carcinogenesis. Thus, these antioxidants modify two-stage chemical carcinogenesis in the forestomach, liver, kidney, urinary bladder, and thyroid, but show organ-specific differences in effects.

L14 ANSWER 32 OF 60 MEDLINE

ACCESSION NUMBER: 83206490 MEDLINE

DOCUMENT NUMBER: 83206490

TITLE: Inhibition by 2(3)-tert-butyl-4-hydroxyanisole and other antioxidants of epidermal ornithine decarboxylase activity **induced** by 12-O-tetradecanoylphorbol-13-acetate.

AUTHOR: Kozumbo W J; Seed J L; Kensler T W

CONTRACT NUMBER: ES07067 (NIEHS)

ES00454 (NIEHS)

SOURCE: CANCER RESEARCH, (1983 Jun) 43 (6) 2555-9.

Journal code: CNF. ISSN: 0008-5472.

PUB. COUNTRY:

United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals; Cancer Journals

ENTRY MONTH:

198309

AB The relationship between reactive oxygen and/or free radical species and tumor promotion was evaluated by investigating the inhibitory effects of 2(3)-tert-butyl-4-hydroxyanisole (BHA) and other antioxidants on the **induction** of ornithine decarboxylase (ODC) activity in mouse epidermis by a tumor **promoter**, 12-O-tetradecanoylphorbol-13-acetate (TPA). Mice maintained on a diet containing 0.75% BHA for 8 days showed a 50% reduction in maximal ODC **induction** following treatment with TPA when compared to mice fed a control diet. Topical application of BHA (55 μ mol) 30 min prior to TPA treatment (17 nmol) elicited an 80% inhibition of **promoter-induced** ODC

activity. BHA was ineffective as an inhibitor when administered either 16 hr before or 2 hr after the **promoter**. The inhibition by BHA was dose dependent with a dose producing a 50% inhibition of ODC **induction** of 6 μmol . A structure-activity study with BHA analogues (2-tert-butyl-4-hydroxyanisole, 3-tert-butyl-4-hydroxyanisole, 2-tert-butyl-1,4-dimethoxybenzene, tert-butylhydroquinone, 4-hydroxyanisole, p-hydroquinone, phenol, and 2-tert-butyl-phenol) showed that hydroxyl and tert-butyl substituents were important determinants of inhibitory activity. A spectrum of other antioxidants were also tested. Butylated hydroxytoluene was nearly equipotent to BHA; alpha-tocopherol, propyl gallate, and disulfiram were all less potent, and L-**ascorbate** was inactive. None of the antioxidants affected basal ODC activity in non-TPA-treated mice. Collectively, these results demonstrate an early and direct inhibition of TPA-**induced** ODC activity by lipophilic phenolic antioxidants and suggest a role for reactive oxygen and/or free radical species in tumor promotion.

L14 ANSWER 33 OF 60 MEDLINE

ACCESSION NUMBER: 81263177 MEDLINE

DOCUMENT NUMBER: 81263177

TITLE: A study of the peroxidation of fatty acid micelles promoted

by ionizing radiation, hydrogen peroxide and ascorbate.

AUTHOR: Yau T M; Mencl J

CONTRACT NUMBER: CA-15901 (NCI)

CA-19283 (NCI)

SOURCE: INTERNATIONAL JOURNAL OF RADIATION BIOLOGY AND RELATED STUDIES IN PHYSICS, CHEMISTRY AND MEDICINE, (1981 Jul) 40 (1) 47-61.

Journal code: GSV. ISSN: 0020-7616.

PUB. COUNTRY: ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198112

AB the kinetics of peroxidation of fatty acid micelles promoted by ionizing radiation, hydrogen peroxide and **ascorbate** were compared. At the dose-rate range of ionizing radiation studied, the higher the dose-rate, the greater the total dose required to produce the same effect. With **ascorbate**, the rate of lipid peroxidation was dependent on the concentration of the **promoter** only up to 1×10^{-4} M, beyond which a decreasing rate of peroxidation **induction** was observed. Higher concentration of **ascorbate** also suppressed the promoting effect of ionizing radiation. Formate, a hydroxyl radical scavenger, inhibited the peroxidation process promoted by these three agents.

Caesium

was found to be slightly inhibitory. EDTA and deoxycholate were also inhibitory, which may be attributed to iron-chelating and micelle-disrupting capacity, respectively. Addition of iron (Fe^{2+} or

Fe^{3+})

to EDTA-chelated fatty acid micelles re-initiated the peroxidation process. The ease of fatty acid oxidation at pH 7.5 was arachidonic

(20:4)

greater than linolenic (18:3) greater than linoleic (18:2). This order

was

reversed at pH 11.5. Similarities in the kinetics of peroxidation

obtained

suggest that certain biological sequelae encountered in cells treated

with

these seemingly dissimilar agents might arise through some common mechanism(s).

L14 ANSWER 34 OF 60 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 2000:312373 CAPLUS

DOCUMENT NUMBER: 133:100791

TITLE: Differences of promoting activity and loss of

heterozygosity between dimethylarsinic acid and sodium

L-ascorbate in F1 rat urinary bladder carcinogenesis
 AUTHOR(S): Chen, Tianxin; Na, Yifei; Wanibuchi, Hideki;
 Yamamoto, Shinji; Lee, Chyi Chia R.; Fukushima, Shoji
 CORPORATE SOURCE: First Department of Pathology, Osaka City University
 Medical School, Osaka, 545-8585, Japan
 SOURCE: Arsenic Exposure Health Eff., Proc. Int. Conf., 3rd
 (1999), Meeting Date 1998, 263-266. Editor(s):
 Chappell, Willard R.; Abernathy, Charles O.;
 Calderon, Rebecca L. Elsevier Science Ltd.: Oxford, UK.
 CODEN: 68YOAM
 DOCUMENT TYPE: Conference
 LANGUAGE: English

AB Dimethylarsinic acid (DMA) is known to have promoting activity on rat urinary bladder carcinogenesis in F344 rats initiated with N-butyl-N-(4-hydroxybutyl)nitrosamine (BBN). Sodium L-ascorbate is also a strong **promoter** in this animal model. In this study, the authors used (Lewis.times.F344)F1 rats to compare the promoting activity between DMA and sodium L-ascorbate and to find mol. alterations in the urinary bladder tumors. Male, 6-wk-old rats were given 0.05% BBN in drinking water for 4 wk, and then the rats were kept with no treatment for group 1, administered 0.01% DMA in drinking water (group 2) or 5% sodium L-ascorbate in the powd. diet (group 3). Group 4 rats were continuously given BBN alone. At weeks 36 and 44, the rats were sacrificed and the urinary bladders were fixed in 10% phosphate buffered formalin and embedded in paraffin. H&E staining was done for histol., and microdissection was done for loss of heterozygosity (LOH) examn. DMA and sodium L-ascorbate showed promoting activity on urinary bladder carcinogenesis of F1 rat, however DMA revealed weaker promotion activity than that of sodium L-ascorbate, although doses were different. LOH existed in the urinary bladder tumors treated with DMA, whereas no LOH was detected in the urinary bladder tumors treated with sodium L-ascorbate.

REFERENCE COUNT: 15
 REFERENCE(S): (1) Braman, R; Science 1973, V182, P1247 CAPLUS
 (4) Chen, T; Teratogen Carcin Mut 1998, V18, P101 CAPLUS
 (5) Dong, J; Mutat Res 1993, V302, P97 CAPLUS
 (6) Endo, G; Bull Environ Contam Toxicol 1992, V48, P131 CAPLUS
 (7) Fukushima, S; Acta Pathol Jpn 1982, V32, P243 CAPLUS
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 35 OF 60 CAPLUS COPYRIGHT 2000 ACS
 ACCESSION NUMBER: 2000:55404 CAPLUS
 DOCUMENT NUMBER: 132:163537
 TITLE: Stress **induction** of a nuclear gene encoding for a plastid protein is mediated by photo-oxidative events
 AUTHOR(S): Manac'h, Nathalie; Kuntz, Marcel
 CORPORATE SOURCE: Genetique moleculaire des plantes, CNRS/UMR 5575, Grenoble, 38041, Fr.
 SOURCE: Plant Physiol. Biochem. (Paris) (1999), 37(11), 859-868
 CODEN: PPBIEX; ISSN: 0981-9428
 PUBLISHER: Editions Scientifiques et Medicales Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Fibrillin was originally identified as a chromoplast protein involved in the assembly of carotenoid-contg. fibrils and was also found to accumulate

in chloroplasts of wounded or water-stressed leaves. It is shown that the promoter from the pepper fibrillin (nuclear) gene can be **induced** in leaves of stable tomato transformants by various stresses, namely wounding, drought, cold and salt stress, in light but not in darkness, as well as by high light intensities. Various herbicides causing reactive oxygen (superoxide, singlet oxygen) prodn. in chloroplasts also **induce** the promoter. Higher expression levels are obsd. in transgenic tobacco plants which are apparently more sensitive to photo-oxidative stress than tomato. Similarly, wounding which causes strong **induction** of the promoter in tobacco, produces only weak **induction** in tomato. Hydrogen peroxide produced in plastids or added exogenously causes the **induction** of this nuclear gene. The data suggest that the **ascorbate**/glutathione pathway (which eliminates hydrogen peroxide) can influence indirectly the **induction** of the fibrillin **promoter**. A generalized model is proposed which links stresses of external origin to nuclear gene **induction**, via the plastid compartment which is subjected to photo-oxidative stress.

REFERENCE COUNT: 31
 REFERENCE(S): (3) Banzet, N; Plant J 1998, V13, P519 CAPLUS
 (5) Chamnongpol, S; Proc Natl Acad Sci USA 1998, V95, P5818 CAPLUS
 (6) Chen, G; Plant Cell Physiol 1989, V30, P987
 CAPLUS
 (7) Chen, H; Plant J 1998, V14, P317 CAPLUS
 (8) Deruere, J; Biochem Biophys Res Commun 1994, V199, P1144 CAPLUS
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 36 OF 60 CAPLUS COPYRIGHT 2000 ACS
 ACCESSION NUMBER: 1999:690874 CAPLUS
 DOCUMENT NUMBER: 131:318573
 TITLE: Transgenic cucumber that produces high levels of superoxide dismutase for use in cosmetics and as food additives
 INVENTOR(S): Kim, Jae-whune; Lee, Haeng-soon; Kwon, Suk Yoon; Kwak, Sang Soo
 PATENT ASSIGNEE(S): Korea Institute of Science and Technology, S. Korea
 SOURCE: Eur. Pat. Appl., 25 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 952224	A2	19991027	EP 1999-302909	19990414
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 11341929	A2	19991214	JP 1999-105933	19990413
US 6084152	A	20000704	US 1999-291562	19990414
PRIORITY APPLN. INFO.:			KR 1998-13205	19980414
			KR 1998-33947	19980821
			KR 1999-11848	19990406

AB The present invention relates to transgenic plants that produces high levels of superoxide dismutase (SOD) and to methods for producing said transgenic plants. More particularly, the present invention relates to a transgenic plant and a method, in which the hypocotyl section of seedlings is cocultured with Agrobacterium transformant and regenerated by adventitious shoot **induction** and by root **induction**. Agrobacterium transformant contains an expression vector which comprises

the **promoter** of fruit-dominant **ascorbate** oxidase gene, SOD gene isolated from cassava, and herbicide-resistant bar gene. The present invention also relates to a method for **inducing** adventitious shoots from the hypocotyl section in plant tissue culture, thus providing a method for the efficient prodn. of transgenic plants maintaining higher SOD activity in fruits. Therefore, the SOD transgenic cucumber in the present invention can be used as a material for cosmetics, additives in functional foods, and medicines as well as a plant which has tolerance to herbicides and environmental stresses.

L14 ANSWER 37 OF 60 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:223051 CAPLUS

DOCUMENT NUMBER: 130:265006

TITLE: cDNAs of banana fruit development and the gene products and developmentally-regulated promoter regions

INVENTOR(S): May, Gregory; Clendennen, Stephanie

PATENT ASSIGNEE(S): Boyce Thompson Institute for Plant Research, Inc., USA

SOURCE: PCT Int. Appl., 143 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9915668	A2	19990401	WO 1998-US3343	19980923
WO 9915668	A3	19991007		
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 9894712	A1	19990412	AU 1998-94712	19980923
EP 1017820	A2	20000712	EP 1998-948058	19980923
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			

PRIORITY APPLN. INFO.: US 1997-60062 19970925
WO 1998-US3343 19980923

AB CDNAs from banana fruit development and ripening are cloned and characterized. Gene products and promoter regions of the genes are also characterized. The promoter regions of these genes may be useful in the fruit- or development-specific expression of genes, e.g. of a gene for a therapeutic protein. These promoters may also be ethylene-responsive and easily **induced** by exposure to the gas. Ripening stage-specific genes were identified by differential screening of cDNA banks from different stages of fruit ripening with probes from other stages of ripening. A total of 38 clones falling into 11 sequence classes were identified as showing up- or down-regulation in stages PCI1 and PCI3 of fruit ripening. Putative functions of the gene products were assigned after BLAST searching. One gene appears to encode an acidic chitinase homolog and another a new class of metallothioneins.

L14 ANSWER 38 OF 60 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1998:371512 CAPLUS

DOCUMENT NUMBER: 129:14525

TITLE: Paraquat sensitivity of transgenic *Nicotiana tabacum* plants that overproduce a cytosolic ascorbate peroxidase

AUTHOR(S): Saji, H.; Aono, M.; Kubo, A.; Tanaka, K.; Kondo, N.

CORPORATE SOURCE: National Institute Environmental Studies, Tsukuba, 305, Japan

SOURCE: Phytol (Horn, Austria) (1997), 37(3), 259-264

CODEN: PHYNAZ; ISSN: 0079-2047

PUBLISHER: Verlag Ferdinand Berger & Soehne

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The cDNA encoding the Arabidopsis cytosolic **ascorbate** peroxidase was placed under the control of the **promoter** for ribulose-1,5-bisphosphate carboxylase small subunit gene, and the chimeric gene was then introduced into tobacco. Leaves of the transgenic plants exhibited up to 5 to 10 fold higher ascorbate peroxidase activity than control non-transgenic plants. However, the paraquat sensitivity of these transgenic plants did not differ from that of control plants as evaluated by electrolyte leakage from leaf disks. The ascorbate content of leaf disks of both transgenic and control plants rapidly decreased during paraquat treatment. The cytosolic activity of ascorbate peroxidase appears therefore, at least under the present study conditions, not to be a limiting factor in the tolerance of plants to paraquat-induced oxidative stress.

L14 ANSWER 39 OF 60 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1997:421612 CAPLUS

DOCUMENT NUMBER: 127:133817

TITLE: Ascorbic acid-dependent activation of the osteocalcin promoter in MC3T3-E1 preosteoblasts: requirement for collagen matrix synthesis and the presence of an intact OSE2 sequence

AUTHOR(S): Xiao, Guozhi; Cui, Yingqi; Ducky, Patricia; Karsenty, Gerard; Franceschi, Renny T.

CORPORATE SOURCE: Dep. Periodontics, Prevention, and Geriatrics, Univ. Michigan, Ann Arbor, MI, 48109-1078, USA

SOURCE: Mol. Endocrinol. (1997), 11(8), 1103-1113

CODEN: MOENEN; ISSN: 0888-8809

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Osteocalcin is a hormonally regulated calcium-binding protein made almost exclusively by osteoblasts. In normal cells, osteocalcin expression requires ascorbic acid (AA), an essential cofactor for osteoblast differentiation both in vivo and in vitro. To det. the mechanism of this regulation, subclones of MC3T3-E1 preosteoblasts were transiently transfected with 1.3 kb of the mouse osteocalcin gene 2 promoter driving expression of firefly luciferase. AA stimulated luciferase activity 20-fold after 4-5 days. This response was stereospecific to L-ascorbic acid and was only detected in MC3T3-E1 subclones showing strong AA **induction** of the endogenous osteocalcin gene. Similar results were also obtained in MC3T3-E1 cells stably transfected with the osteocalcin promoter. A specific inhibitor of collagen synthesis, 3,4-dehydroproline, blocked AA-dependent **induction** of promoter activity, indicating that regulation of the osteocalcin gene requires collagen matrix synthesis. Deletion anal. of the mOG2 promoter identified an essential region for AA responsiveness between -147 and -116 bp. This region contains a single copy of the previously described osteoblast-specific element, OSE2. Deletion and mutation of OSE2 in DNA transfection assays established the requirement for this element in the AA response. Furthermore, DNA-binding assays revealed that MC3T3-E1 cells contain OSF2, the nuclear factor binding to OSE2, and that binding of OSF2 to OSE2 is up-regulated by AA treatment. Taken collectively, our results indicate that an intact OSE2 sequence is required for the **induction** of osteocalcin expression by AA.

L14 ANSWER 40 OF 60 USPATFULL

ACCESSION NUMBER: 2000:84488 USPATFULL

TITLE: Method for producing transgenic cucumber that produces high levels of superoxide dismutase

INVENTOR(S): Kwak, Sang Soo, Taejon-si, Korea, Republic of
Kim, Jae-Whune, Taejon-si, Korea, Republic of
Lee, Haeng-Soon, Taejon-si, Korea, Republic of
Kwon, Suk Yoon, Taejon-si, Korea, Republic of

PATENT ASSIGNEE(S): Korea Institute of Science and Technology, Korea,
Republic of (non-U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6084152	20000704
APPLICATION INFO.:	US 1999-291562	19990414 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	KR 1998-13205	19980414
	KR 1998-33947	19980821
	KR 1999-11848	19990406

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Fox, David T.

ASSISTANT EXAMINER: Ibrahim, Medina A.

LEGAL REPRESENTATIVE: Gates & Cooper

NUMBER OF CLAIMS: 17

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 7 Drawing Figure(s); 8 Drawing Page(s)

LINE COUNT: 959

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to a transgenic plant that produces high levels of

superoxide dismutase (SOD) and to a method for producing the transgenic plant. The hypocotyl section of seedlings is co-cultured with Agrobacterium transformant and regenerated by adventitious shoot **induction** and by root **induction**, where the Agrobacterium transformant contains an expression vector that comprises the **promoter** of a fruit-dominant **ascorbate** oxidase gene, an SOD gene isolated from cassava, and an herbicide-resistant bar gene. The present invention also relates to a method for **inducing** adventitious shoot from hypocotyl sections in plant tissue culture, thus providing a method for the efficient production of transgenic plants maintaining higher SOD activity in fruits. Therefore, the SOD transgenic cucumber of the present invention can be used for cosmetics, additives in functional foods, and medicines as well as having tolerance to herbicides and environmental stresses.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 114 ibib abs 41-50

L14 ANSWER 41 OF 60 USPATFULL

ACCESSION NUMBER: 2000:54150 USPATFULL

TITLE: Manipulating nitrosative stress to kill pathologic microbes, pathologic helminths and pathologically proliferating cells or to upregulate nitrosative stress

defenses

INVENTOR(S): Stamler, Jonathan S., Chapel Hill, NC, United States
Griffith, Owen W., Milwaukee, WI, United States

PATENT ASSIGNEE(S): Duke University, Durham, NC, United States (U.S. corporation)
The Medical College of Wisconsin Research Foundation,

	NUMBER	DATE
PATENT INFORMATION:	US 6057367	20000502
APPLICATION INFO.:	US 1997-852490	19970507 (8)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-25819	19960830 (60)
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Weddington, Kevin E.	
NUMBER OF CLAIMS:	66	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	2 Drawing Figure(s); 2 Drawing Page(s)	
LINE COUNT:	3415	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Mammals are treated for infections or for conditions associated with pathologically proliferating mammalian cell growth (for example, certain cancers, restenosis, benign prostatic hypertrophy) by administration of a manipulator of nitrosative stress to selectively kill or reduce the growth of the microbes or helminths causing the infection or of host cells infected with the microbes or of the pathologically proliferating mammalian cells. Novel agents include .alpha.-alkyl-S-alkyl-homocysteine sulfoximines wherein the .alpha.-alkyl contains 2 to 8 carbon atoms, and the S-alkyl-contains 1 to 10 carbon atoms. In another invention herein, mammals in need of increased nitrosative stress defenses are treated, e.g., humans at risk for a stroke because of having had a transient ischemic attack, are treated. Treatments to increase nitrosative stress defenses include, for example, repeated administrations of low doses of manipulators of nitrosative stress so that the subject treated has increased tolerance to nitrosative stress. In still another invention, mammals are treated for protozoal infections by systemic administration of L-buthionine-S-sulfoximine and agent that increases nitrosative stress.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 42 OF 60 USPATFULL
 ACCESSION NUMBER: 2000:5020 USPATFULL
 TITLE: Molecular methods of hybrid seed production
 INVENTOR(S): Fabijanski, Steven F., Ontario, Canada
 Albani, Diego, Norfolk, United Kingdom
 Robert, Laurian S., Ottawa, Canada
 Arnison, Paul G., Ontario, Canada
 PATENT ASSIGNEE(S): Pioneer Hi-Bred International, Inc., Des Moines, IA,
 United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6013859	20000111
APPLICATION INFO.:	US 1995-476864	19950607 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1994-276510, filed on 14 Jul 1994 which is a continuation of Ser. No. US 556917	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Fox, David T.	
LEGAL REPRESENTATIVE:	Foley & Lardner	
NUMBER OF CLAIMS:	23	
EXEMPLARY CLAIM:	1,11	
NUMBER OF DRAWINGS:	30 Drawing Figure(s); 78 Drawing Page(s)	
LINE COUNT:	4621	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A process is described for producing fertile hybrid seed or hybrid seed

comprising fertile and sterile seed using male-sterile plants created
by
employing molecular techniques to manipulate genes that are capable of
controlling the production of fertile pollen in plants. Hybrid seed
production is simplified and improved by this approach, which can be
extended to plant crop species for which commercially acceptable hybrid
seed production methods have not been available.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 43 OF 60 USPATFULL

ACCESSION NUMBER: 1999:150949 USPATFULL
TITLE: Assays to identify **inducers** of plant defense
resistance
INVENTOR(S): Klessig, Daniel Frederick, Bridgewater, NJ, United
States
Chen, Zhixiang, Highland Park, NJ, United States
PATENT ASSIGNEE(S): Rutgers, The State University of New Jersey, New
Brunswick, NJ, United States (U.S. corporation)

	NUMBER	DATE
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PATENT INFORMATION:	US 5989846	19991123
APPLICATION INFO.:	US 1995-470769	19950606 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1995-418554, filed on 7 Apr 1995, now abandoned which is a continuation-in-part of Ser. No. US 1994-259535, filed on 14 Jun 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-146317, filed on 2 Nov 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-38132, filed on 26 Mar 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-923229, filed on 31 Jul 1992, now abandoned	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Gitomer, Ralph	
LEGAL REPRESENTATIVE:	Lerner, David, Littenberg, Krumholz & Mentlik	
NUMBER OF CLAIMS:	4	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	26 Drawing Figure(s); 15 Drawing Page(s)	
LINE COUNT:	2763	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		
AB	The present invention relates to assays which can be used to identify inducers of plant resistance to pathogens. The assays use catalase and/or ascorbate peroxidase.	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 44 OF 60 USPATFULL

ACCESSION NUMBER: 1999:92566 USPATFULL
TITLE: Methods and compositions of growth control for cells
encapsulated within bioartificial organs
INVENTOR(S): Schinstine, Malcolm, Bristol, RI, United States
Shoichet, Molly S., Canton, MA, United States
Gentile, Frank T., Warwick, RI, United States
Hammang, Joseph P., Barrington, RI, United States
Holland, Laura M., Providence, RI, United States
Cain, Brian M., Everett, MA, United States
Doherty, Edward J., Mansfield, MA, United States
Winn, Shelley R., Smithfield, RI, United States
Aebischer, Patrick, Lutry, Switzerland
PATENT ASSIGNEE(S): CytoTherapeutics, Inc., United States (U.S.
corporation)

	NUMBER	DATE
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PATENT INFORMATION:	US 5935849	19990810

APPLICATION INFO.: US 1994-279773 19940720 (8)
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Achutamurthy, Ponnathapura
LEGAL REPRESENTATIVE: Elrifi, Ivor R.; Morency, MichelMintz, Levin
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1,5
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT: 2234

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to methods and compositions of controlling cell distribution within a bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a growth surface within the bioartificial organ. Such treatments include (1) genetically manipulating cells, (2) exposing the cells to a proliferation-inhibiting compound or a differentiation-**inducing** compound or removing the cells from exposure to a proliferation-stimulating compound or a differentiation-inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the BAO with ECM molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 45 OF 60 USPATFULL

ACCESSION NUMBER: 1999:4408 USPATFULL
TITLE: Control of cell growth in a bioartificial organ with extracellular matrix coated microcarriers
INVENTOR(S): Schinstine, Malcolm, Ben Salem, PA, United States
Shoichet, Molly S., Toronto, Canada
Gentile, Frank T., Warwick, RI, United States
Hammang, Joseph P., Barrington, RI, United States
Holland, Laura M., Horsham, PA, United States
Cain, Brian M., Everett, MA, United States
Doherty, Edward J., Mansfield, MA, United States
Winn, Shelley R., Smithfield, RI, United States
Aebischer, Patrick, Lutry, Switzerland
PATENT ASSIGNEE(S): CytoTherapeutics, Inc., United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5858747	19990112
APPLICATION INFO.:	US 1995-447810	19950523 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1995-432698, filed on 9 May 1995 which is a continuation-in-part of Ser. No. US 1994-279773, filed on 20 Jul 1994	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Naff, David M.	
LEGAL REPRESENTATIVE:	Elrifi, Ivor R.Mintz, Levin	
NUMBER OF CLAIMS:	11	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 5 Drawing Page(s)	
LINE COUNT:	2333	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods and compositions are provided for controlling cell distribution within an implantable bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a growth surface within the bioartificial organ. Such treatments include (1) genetically manipulating cells, (2) exposing the cells to a proliferation-inhibiting compound or a differentiation-**inducing** compound or removing the cells from exposure to a proliferation-stimulating compound or a

differentiation-inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the bioartificial organ with extracellular matrix molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination. The bioartificial organ typically has a semipermeable membrane encapsulating a cell-containing core, and is preferably immunoisulatory. Cells can be grown on microcarriers and then loaded into the bioartificial organ. The microcarriers may be coated with an extracellular matrix component such as collagen to cause decreased cell proliferation or increased cell differentiation. Microcarriers containing cells can be suspended in a proliferation inhibiting hydrogel matrix prior to encapsulation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 46 OF 60 USPATFULL

ACCESSION NUMBER: 1998:161993 USPATFULL
 TITLE: Methods and compositions of growth control for cells encapsulated within bioartificial organs
 INVENTOR(S): Schinstine, Malcolm, Ben Salem, PA, United States
 Shoichet, Molly S., Toronto, Canada
 Gentile, Frank T., Warwick, RI, United States
 Hammang, Joseph P., Barrington, RI, United States
 Holland, Laura M., Horsham, PA, United States
 Cain, Brian M., Everett, MA, United States
 Doherty, Edward J., Mansfield, MA, United States
 Winn, Shelley R., Smithfield, RI, United States
 Aebischer, Patrick, Lutry, Canada
 PATENT ASSIGNEE(S): CytoTherapeutics, Inc., Lincoln, RI, United States
 (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5853717	19981229
APPLICATION INFO.:	US 1995-447356	19950523 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1995-432698, filed on 9 May 1995 which is a continuation-in-part of Ser. No. US 1994-279773, filed on 20 Jul 1994	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Ketter, James	
ASSISTANT EXAMINER:	Yucel, Irem	
LEGAL REPRESENTATIVE:	Morency, Michel; Elrifi, Ivor R.; Levin, Mintz	
NUMBER OF CLAIMS:	14	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 5 Drawing Page(s)	
LINE COUNT:	2340	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to methods and compositions of controlling cell distribution within a bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a growth surface within the bioartificial organ. Such treatments include (1) genetically manipulating cells, (2) exposing the cells to a proliferation-inhibiting compound or a differentiation-inducing compound or removing the cells from exposure to a proliferation-stimulating compound or a differentiation-inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the BAO with ECM molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 47 OF 60 USPATFULL

ACCESSION NUMBER: 1998:150454 USPATFULL
 TITLE: Controlling proliferation of cells before and after encapsulation in a bioartificial organ by gene transformation
 INVENTOR(S): Schinstine, Malcolm, Ben Salem, PA, United States
 Shoichet, Molly S., Toronto, Canada
 Gentile, Frank T., Warwick, RI, United States
 Hammang, Joseph P., Barrington, RI, United States
 Holland, Laura M., Horsham, PA, United States
 Cain, Brian M., Everett, MA, United States
 Doherty, Edward J., Mansfield, MA, United States
 Winn, Shelley R., Smithfield, RI, United States
 Aebischer, Patrick, Lutry, Switzerland
 PATENT ASSIGNEE(S): CytoTherapeutics, Inc., United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5843431	19981201
APPLICATION INFO.:	US 1995-432698	19950509 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1994-279773, filed on 20 Jul 1994	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Naff, David M.	
LEGAL REPRESENTATIVE:	Elrifi, Ivor R. Mintz, Levin	
NUMBER OF CLAIMS:	10	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 5 Drawing Page(s)	
LINE COUNT:	2352	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods and compositions are provided for controlling cell distribution within an implantable bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a growth surface within the bioartificial organ. Such treatments include (1) genetically manipulating cells, (2) exposing the cells to a proliferation-inhibiting compound or a differentiation-inducing compound or removing the cells from exposure to a proliferation-stimulating compound or a differentiation-inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the bioartificial organ with extracellular matrix molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination. Cells can be transformed with a proliferation-promoting gene such as the oncogene, SV40, linked to a regulatable promoter such as the Mx1 promoter, the promoter is activated in vitro to express the gene to result in cell proliferation, and the promoter is inactivated before or after insertion of the cells in the bioartificial organ to inhibit expression of the gene to reduce or stop cell proliferation in vivo. The promoter can be reactivated in vivo to again express the gene to result in further cell proliferation. The gene may be a proliferation-suppressing gene such as p53 gene or RB gene, or a differentiation-inducing gene such as high mobility group chromosomal protein 14. Inhibiting gene expression in vitro causes cell proliferation, and inducing gene expression reduces or stops cell proliferation in vivo.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 48 OF 60 USPATFULL
 ACCESSION NUMBER: 1998:147298 USPATFULL
 TITLE: Methods and compositions of growth control for cells encapsulated within bioartificial organs
 INVENTOR(S): Schinstine, Malcolm, Ben Salem, PA, United States

Shoichet, Molly S., Toronto, Canada
 Gentile, Frank T., Warwick, RI, United States
 Hammang, Joseph P., Barrington, RI, United States
 Holland, Laura M., Horsham, PA, United States
 Cain, Brian M., Everett, MA, United States
 Doherty, Edward J., Mansfield, MA, United States
 Winn, Shelley R., Smithfield, RI, United States
 Aebischer, Patrick, Lutry, Switzerland
 PATENT ASSIGNEE(S): CytoTherapeutics, Inc., United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5840576	19981124
APPLICATION INFO.:	US 1995-445193	19950523 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1995-432698, filed on 9 May 1995 which is a continuation-in-part of Ser. No. US 1994-279773, filed on 20 Jul 1994	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Archutamurthy, Ponnathapura	
LEGAL REPRESENTATIVE:	Elrifi, Ivor R.; Levin, Mintz	
NUMBER OF CLAIMS:	4	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 5 Drawing Page(s)	
LINE COUNT:	2293	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to methods and compositions of controlling cell distribution within a bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a growth surface within the bioartificial organ. Such treatments include (1) genetically manipulating cells, (2) exposing the cells to a proliferation-inhibiting compound or a differentiation-inducing compound or removing the cells from exposure to a proliferation-stimulating compound or a differentiation-inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the BAO with ECM molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 49 OF 60 USPATFULL

ACCESSION NUMBER: 1998:138431 USPATFULL
 TITLE: Methods and compositions of growth control for cells encapsulated within bioartificial organs
 INVENTOR(S): Schinstine, Malcolm, Ben Salem, PA, United States
 Shoichet, Molly S., Toronto, Canada
 Gentile, Frank T., Warwick, RI, United States
 Hammang, Joseph P., Barrington, RI, United States
 Holland, Laura M., Horsham, PA, United States
 Cain, Brian M., Everett, MA, United States
 Doherty, Edward J., Mansfield, MA, United States
 Winn, Shelley R., Smithfield, RI, United States
 Aebischer, Patrick, Lutry, Switzerland
 PATENT ASSIGNEE(S): CytoTherapeutics, Inc., Lincoln, RI, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5833979	19981110
APPLICATION INFO.:	US 1995-447771	19950523 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1995-432698, filed on 9 May 1995 which is a continuation-in-part of Ser. No. US 1994-279773, filed on 20 Jul 1994	

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Ketter, James
ASSISTANT EXAMINER: Yucel, Irem
LEGAL REPRESENTATIVE: Elrifi, Ivor R.; Levin, Mintz
NUMBER OF CLAIMS: 2
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT: 2266

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to methods and compositions of controlling cell distribution within a bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a growth surface within the bioartificial organ. Such treatments include (1) genetically manipulating cells, (2) exposing the cells to a proliferation-inhibiting compound or a differentiation-inducing compound or removing the cells from exposure to a proliferation-stimulating compound or a differentiation-inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the BAO with ECM molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L14 ANSWER 50 OF 60 USPATFULL

ACCESSION NUMBER: 1998:98815 USPATFULL

TITLE: Method for controlling proliferation and differentiation of cells encapsulated within bioartificial organs

INVENTOR(S): Schinstine, Malcolm, Ben Salem, PA, United States
Shoichet, Molly S., Toronto, Canada
Gentile, Frank T., Warwick, RI, United States
Hammang, Joseph P., Barrington, RI, United States
Holland, Laura M., Horsham, PA, United States
Cain, Brian M., Everett, MA, United States
Doherty, Edward J., Mansfield, MA, United States
Winn, Shelley R., Smithfield, RI, United States
Aebischer, Patrick, Lutry, Switzerland

PATENT ASSIGNEE(S): Cytotherapeutics, Inc., Lincoln, RI, United States
(U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5795790	19980818
APPLICATION INFO.:	US 1995-448201	19950523 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1995-432698, filed on 9 May 1995 which is a continuation-in-part of Ser. No. US 1994-279773, filed on 20 Jul 1994	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Naff, David M.	
LEGAL REPRESENTATIVE:	Mintz, Levin, Cohn, Ferris, Glovsky and Popeo; Elrifi, Ivor R.	
NUMBER OF CLAIMS:	10	
EXEMPLARY CLAIM:	6	
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 5 Drawing Page(s)	
LINE COUNT:	2311	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods and compositions are provided for controlling cell distribution within a bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a growth surface within the bioartificial organ.

Such treatments include (1) genetically manipulating cells, (2) exposing the cells to a proliferation-inhibiting compound or a differentiation-

inducing compound or removing the cells from exposure to a proliferation-stimulating compound or a differentiation-inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the bioartificial organ with extracellular matrix molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination. In a preferred treatment, cells are exposed to and then removed from exposure to a proliferation-stimulating and differentiation inhibiting compound prior to encapsulation of the cells in a semipermeable biocompatible jacket to form a bioartificial organ. Upon in vivo implantation of the bioartificial organ in a host, cellular proliferation is inhibited and cellular differentiation is promoted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> s ascorbate and reporter

L15 112 ASCORBATE AND REPORTER

=> s ascorbate (p) reporter

L16 39 ASCORBATE (P) REPORTER

=> dup rem l16

PROCESSING COMPLETED FOR L16

L17 15 DUP REM L16 (24 DUPLICATES REMOVED)

=> d l17 ibib abs tot

L17 ANSWER 1 OF 15 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000424117 MEDLINE
DOCUMENT NUMBER: 20361782
TITLE: Dissemination of peroxidative stress via intermembrane transfer of lipid hydroperoxides: model studies with cholesterol hydroperoxides.
AUTHOR: Vila A; Korytowski W; Girotti A W
CORPORATE SOURCE: Department of Biochemistry, Medical College of Wisconsin, Milwaukee, Wisconsin 53226, USA.
CONTRACT NUMBER: CA72630 (NCI)
F31CA85171 (NCI)
SOURCE: ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, (2000 Aug 1) 380 (1) 208-18.
Journal code: 6SK. ISSN: 0003-9861.
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ENTRY MONTH: 200011
ENTRY WEEK: 20001102
AB Lipid hydroperoxides (LOOHs) can be generated in cells when cholesterol (Ch) and other unsaturated lipids in cell membranes are degraded under conditions of oxidative stress. If LOOHs escape reductive detoxification by glutathione-dependent selenoperoxidases, they may undergo iron-catalyzed one-electron reduction to free radical species, thus triggering peroxidative chain reactions which exacerbate oxidative membrane damage. LOOHs are more polar than parent lipids and much longer-lived than free radical precursors or products. Accordingly, intermembrane transfer of LOOHs (analogous to that of unoxidized precursors) might be possible, and this could jeopardize acceptor membranes. We have investigated this possibility, using photoperoxidized [(14)C]Ch-labeled erythrocyte ghosts as cholesterol hydroperoxide (ChOOH) donors and unilamellar liposomes [e.g., dimyristoyl-

phosphatidylcholine/Ch, 9:1 mol/mol] as acceptors. ChOOH material consisted mainly of 5alpha-hydroperoxide, a singlet oxygen adduct. Time-dependent transfer of ChOOH versus Ch at 37 degrees C was determined, using high-performance liquid and thin-layer chromatographic methods to analyze liposomal extracts for these species. A typical experiment in which the starting ChOOH/Ch mol ratio in ghosts was approximately 0.05 showed that the initial transfer rate of ChOOH was approximately 16 times greater than that of parent Ch. Using [(14)C]Ch as a **reporter** in liposome acceptors, we found that transfer-acquired ChOOHs, when exposed to a lipophilic iron chelate and **ascorbate**, could trigger strong peroxidative chain reactions, as detected by accumulation of [(14)C]Ch oxidation products. These findings support the hypothesis that intermembrane transfer of ChOOHs can contribute to their prooxidant membrane damaging and cytotoxic potential. Copyright 2000 Academic Press.

L17 ANSWER 2 OF 15 MEDLINE DUPLICATE 2
 ACCESSION NUMBER: 1999368250 MEDLINE
 DOCUMENT NUMBER: 99368250
 TITLE: An unusual cytochrome o'-type cytochrome c oxidase in a Bacillus cereus cytochrome a3 mutant has a very high affinity for oxygen.
 AUTHOR: Contreras M L; Escamilla J E; Del Arenal I P; Davila J R; D'mello R; Poole R K
 CORPORATE SOURCE: Depto de Bioquimica, Facultad de Medicina, Universidad Nacional Autonoma de Mexico, D.F., Mexico.
 SOURCE: MICROBIOLOGY, (1999 Jul) 145 (Pt 7) 1563-73.
 Journal code: BXW. ISSN: 1350-0872.
 PUB. COUNTRY: ENGLAND: United Kingdom
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200001
 ENTRY WEEK: 20000104
 AB Bacillus cereus strain PYM1 is a mutant unable to synthesize haem A or spectrally detectable cytochromes aa3 or caa3. The nature of the remaining oxidase(s) catalysing oxygen uptake has been studied. Respiratory oxidase activities and the levels of cytochromes b and c increased 2.6- to 4.2-fold on transition from exponential growth, in either of two media, to sporulation stage III, as previously observed for the parent wild-type strain. NADH oxidase activity at both stages of culture was several-fold higher than **ascorbate** plus tetramethyl-p-phenylenediamine (TMPD) oxidase activity, consistent with the TMPD- phenotype of strain PYM1. Oxidase activity with **ascorbate** as substrate was significant even in the absence of TMPD as electron mediator, suggesting that the terminal oxidase receives electrons from a cytochrome c. Carbon monoxide (CO) difference spectra of membranes were obtained using various reductants (**ascorbate** +/- TMPD, NADH, dithionite) and revealed a haemoprotein resembling cytochrome o'. The CO complex of this cytochrome was photodissociable: the photodissociation spectrum (photolysed minus CO-ligated) exhibited a trough at 416 nm and a peak at 436 nm, together with minor features in the alpha/beta region of the spectrum, consistent with the presence of a cytochrome o'-like pigment. CO recombination occurred at -85 to -95 degrees C. No other haemoproteins showing photoreversible CO binding under these conditions were detected. Evidence that this pigment was the oxidase responsible for substrate oxidation was obtained by photodissociating the CO complex at subzero temperatures in the presence of oxygen; this resulted in faster ligand recombination, attributed to oxygen binding, and extensive oxidation of cytochromes c and b. The oxygen affinity of the oxidase was determined by using the deoxygenation of oxyleghaemoglobin as a sensitive **reporter** of dissociated oxygen concentration. A single oxidase was revealed with a K(m) for oxygen of about 8 nM; this is one of the highest affinities yet

reported for a terminal oxidase.

L17 ANSWER 3 OF 15 MEDLINE
ACCESSION NUMBER: 2000013868 MEDLINE
DOCUMENT NUMBER: 20013868
TITLE: Singlet oxygen adducts of cholesterol: photogeneration and reductive turnover in membrane systems.
AUTHOR: Korytowski W; Girotti A W
CORPORATE SOURCE: Institute of Molecular Biology, Jagiellonian University, Krakow, Poland.
CONTRACT NUMBER: CA70823 (NCI)
CA72630 (NCI)
TW00424 (FIC)
SOURCE: PHOTOCHEMISTRY AND PHOTOBIOLOGY, (1999 Oct) 70 (4) 484-9.

Journal code: P69. ISSN: 0031-8655.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
ENTRY MONTH: 200002
ENTRY WEEK: 20000204

AB Identification of signature products provides a powerful means for establishing whether singlet molecular oxygen (1O_2) is a reactive intermediate in a photodynamic process. This approach is particularly attractive for biological systems in which direct physical measurement is difficult because of the short lifetime of 1O_2 . Among the many possible **reporter** molecules in a target system, cholesterol (Ch) has the advantage of affording a limited number of readily distinguishable oxidation products, among which are the hydroperoxides 3 beta-hydroxy-5 alpha-cholest-6-ene-5-hydroperoxide (5 alpha-OOH), 3 beta-hydroxycholest-4-ene-6 alpha-hydroperoxide (6 alpha-OOH) and 3 beta-hydroxycholest-4-ene-6 beta-hydroperoxide (6 beta-OOH) that derive specifically from 1O_2 addition. The purpose of this study was to compare these species in terms of (1) rates of accumulation in photodynamically treated liposomal membranes; (2) susceptibility to iron-mediated $1 e^-$ reduction that triggers chain peroxidative damage; (3) susceptibility to selenoperoxidase (phospholipid hydroperoxide glutathione peroxidase [PHGPX])-mediated $2 e^-$ reduction that protects against such damage and (4) relative toxicity to mammalian cells. Our results indicate that 5 alpha-OOH is photogenerated at a much greater initial rate than 6 alpha-OOH or 6 beta-OOH. Although liposomal 5 alpha-OOH, 6 alpha-OOH, and 6 beta-OOH exhibit similar first-order decay kinetics during iron/**ascorbate** treatment, the former decays much more slowly during GSH/PHGPX treatment, and is more toxic to L1210 cells. These and related findings suggest that 5 alpha-OOH is potentially the most damaging $CHOOH$ to arise in photodynamically treated cells.

L17 ANSWER 4 OF 15 MEDLINE
ACCESSION NUMBER: 2000058358 MEDLINE
DOCUMENT NUMBER: 20058358
TITLE: Direct observation of stress response in *Caenorhabditis elegans* using a reporter transgene.
AUTHOR: Link C D; Cypser J R; Johnson C J; Johnson T E
CORPORATE SOURCE: Institute for Behavioral Genetics, University of Colorado Boulder 80309-0447, USA.. linkc@colorado.edu
CONTRACT NUMBER: AG12423 (NIA)
P01-AG08761 (NIA)
K02-AA00195 (NIAAA)
+
SOURCE: CELL STRESS AND CHAPERONES, (1999 Dec) 4 (4) 235-42.
Journal code: CV5. ISSN: 1355-8145.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY WEEK: 20000204

AB Transgenic *Caenorhabditis elegans* expressing jellyfish Green Fluorescent Protein under the control of the promoter for the inducible small heat shock protein gene *hsp-16-2* have been constructed. Transgene expression parallels that of the endogenous *hsp-16* gene, and, therefore, allows direct visualization, localization, and quantitation of *hsp-16* expression in living animals. In addition to the expected upregulation by heat shock,

we show that a variety of stresses, including exposure to superoxide-generating redox-cycling quinones and the expression of the human beta amyloid peptide, specifically induce the **reporter** transgene. The quinone induction is suppressed by coinubation with L-**ascorbate**. The ability to directly observe the stress response in living animals significantly simplifies the identification of both exogenous treatments and genetic alterations that modulate stress response, and possibly life span, in *C. elegans*.

L17 ANSWER 5 OF 15 MEDLINE DUPLICATE 5

ACCESSION NUMBER: 1999262050 MEDLINE
DOCUMENT NUMBER: 99262050
TITLE: Radiolabeled cholesterol as a reporter for assessing one-electron turnover of lipid hydroperoxides.
AUTHOR: Korytowski W; Wrona M; Girotti A W
CORPORATE SOURCE: Department of Biochemistry, Medical College of Wisconsin, Milwaukee, Wisconsin 53226, USA.
CONTRACT NUMBER: CA70823 (NCI)
CA72630 (NCI)
TW00424 (FIC)
SOURCE: ANALYTICAL BIOCHEMISTRY, (1999 May 15) 270 (1) 123-32.
Journal code: 4NK. ISSN: 0003-2697.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY WEEK: 19990904

AB A novel approach for assessing the peroxidative chain initiation potency of lipid hydroperoxides has been developed, which involves use of ¹⁴C-labeled cholesterol (Ch) as a "**reporter**" lipid. Unilamellar liposomes containing 1-palmitoyl-2-oleoyl-phosphatidylcholine, [¹⁴C]Ch, and 3beta-hydroxy-5alpha-cholest-6-ene-5-hydroperoxide (5alpha-OOH) or 3beta-hydroxycholest-5-ene-7alpha-hydroperoxide (7alpha-OOH) [100:75:5, mol/mol] were used as a test system. Liposomes incubated in the presence of **ascorbate** and a lipophilic iron complex were analyzed for radiolabeled oxidation products/intermediates (ChOX) by means of silica gel high-performance thin layer chromatography with phosphorimaging detection. The following ChOX were detected and quantified: 7alpha-OOH, 7beta-OOH, 7alpha-OH, 7beta-OH, and 5, 6-epoxide. Total ChOX yield increased in essentially the same time- and [iron]-dependent fashion for initiating 5alpha-OOH and 7alpha-OOH. The initial rate of [¹⁴C]7alphabeta-OH formation was greatly diminished when GSH and ebselen (a selenoperoxidase mimetic) were present, consistent with the

attenuation

of one-electron peroxide turnover. [¹⁴C]Ch-labeled L1210 cells also accumulated ChOX when incubated with 5alpha-OOH-containing liposomes. The rate of accumulation was substantially greater for Se-deficient than Se-sufficient cells, indicating that peroxide-induced chain reactions

were

modulated by selenoperoxidase action. These results illustrate the advantages of the new approach for highly sensitive in situ monitoring of cellular peroxidative damage. Copyright 1999 Academic Press.

L17 ANSWER 6 OF 15 MEDLINE DUPLICATE 6

ACCESSION NUMBER: 2000155705 MEDLINE

DOCUMENT NUMBER: 20155705
TITLE: Cd-induced oxidative burst in tobacco BY2 cells: time course, subcellular location and antioxidant response.
AUTHOR: Piqueras A; Olmos E; Martinez-Solano J R; Hellin E
CORPORATE SOURCE: Departamento de Nutricion y Fisiologia Vegetal, Centro de Edafologia y Biologia Aplicada del Segura (CSIC) Murcia, Spain.
SOURCE: FREE RADICAL RESEARCH, (1999 Dec) 31 Suppl S33-8. Journal code: BW3. ISSN: 1071-5762.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY WEEK: 20000601

AB The relation between Cd and oxidative stress in BY2 cell cultures of tobacco was studied. In response to 5 mM Cd, a rapid generation of H₂O₂ has been detected in tobacco cell cultures by the oxidative quenching of the fluorescent **reporter** dye pyranine. This oxidative burst reached the maximum production of H₂O₂ after 10 min of treatment with Cd. This response could be considered as short term hypersensitive response previous to the oxidative stress caused by the metal at the cell plasma membrane. The observed antioxidant enzymatic response to the oxidative burst was preceded by an increased peroxidation of lipids with a significant increase in the activities of superoxide dismutase and **ascorbate** peroxidase. The results presented in this study point out to the plasma membrane as the primary target for the short term production of activated oxygen species in response to Cd in BY2 tobacco cells followed by a coordinated activation of the antioxidant enzymatic system.

L17 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1998:172907 CAPLUS
DOCUMENT NUMBER: 128:254277
TITLE: Design and Synthesis of a Transition Metal Responsive Semisynthetic Myoglobin-Bearing Iminodiacetic Acid Moiety
AUTHOR(S): Hamachi, Itaru; Matsugi, Tomoaki; Wakigawa, Kengo; Shinkai, Seiji
CORPORATE SOURCE: Department of Chemistry Biochemistry Graduate School of Engineering, Kyushu University, Fukuoka, 812-8581, Japan
SOURCE: Inorg. Chem. (1998), 37(7), 1592-1597
CODEN: INOCAJ; ISSN: 0020-1669
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Iminodiacetic acid appended myoglobins (IDAn-Mb, n = 1, 2) were synthesized by conventional reconstitution of chem. modified hemes with apomyoglobin. The metal responsive property of the obtained IDAn-Mb was studied by metal ion titrn., pH titrn., CD and ¹H NMR spectroscopies, and redn. with **ascorbate**. IDAn-Mb quant. bound various transition metal cations (Co²⁺, Ni²⁺, Zn²⁺, Cd²⁺, and Cu²⁺) but not Mg²⁺. The binding stoichiometry of IDA2-Mb was 1:1 for Co²⁺, Ni²⁺, Zn²⁺, and Cd²⁺ and 1:2 for Cu²⁺, whereas the stoichiometry of 1:1 was shown for IDA1-Mb to all transition metals (Co²⁺, Ni²⁺, Zn²⁺, Cd²⁺, and Cu²⁺). The acidic pK_a shift of the H₂O coordinated to the heme iron(III) was clearly obsd. upon the binding of transition metals, suggesting the microenvironmental change of the heme crevice. This was supported by the CD and ¹H NMR spectra of IDAn-Mb. The transition metal induced structural changes of IDAn-Mb were reflected in their redox behavior, i.e., the redn. rate of IDA2-Mb by **ascorbate** was enhanced 8-fold upon the Co²⁺ binding. The rate showed a good linear relation with the shifted pK_a of the axial H₂O, indicating that the transition metal binding directly affects the electron acceptability of IDAn-Mb. Iminodiacetic acid moieties can play

crucial role as a **reporter** mol. for design of a transition metal responsive semisynthetic protein.

L17 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1998:272639 CAPLUS
DOCUMENT NUMBER: 129:51139
TITLE: Molecular dynamics and phase transitions in phospholipid monolayers at liquid-liquid interfaces
AUTHOR(S): Dzikovskii, B. G.; Livshits, V. A.
CORPORATE SOURCE: N. N. Semenov Institute of Chemical Physics, Russian Academy of Sciences, Moscow, 117334, Russia
SOURCE: Russ. Chem. Bull. (1998), 47(3), 402-410
CODEN: RCBUEY; ISSN: 1066-5285
PUBLISHER: Consultants Bureau
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Stable n-hexadecane/water and n-tetradecane/water macroemulsions contg. monolayers of natural (egg yolk lecithin, EY) and synthetic (dimyristoylphosphatidylcholine, DMPC) phospholipids at liq.-liq. interfaces were prepd. The existence of the monolayers was proved by studying the redn. kinetics of a surface-active spin probe with **ascorbate** anions. Spin labeled derivs. of stearic acid in which the nitroxide group is located at different distances from the polar head (5-, 12-, and 16-doxylstearic acids) were used to study the temp. dependences of the mol. ordering, rotational mobility, and local polarity in the monolayers in emulsions and also in bilayers in liposomes obtained from the same lipids. In the EY monolayers, the degree of spin probe solubilization is higher, while the order parameters (S) and rotational correlation times (.tau.) are lower than those in EY bilayers. The differences between these parameters for mono- and bilayers increase with an increase in the distance of the **reporter** group from the aq. phase. In the DMPC monolayers, a first-order phase transition was detected by measuring the temp. dependences of S and .tau.. The temp. region of the phase transition in monolayers is shifted to lower temps. with respect to that for bilayers and depends on the nature of the oil phase. It was concluded that the phospholipid monolayers in emulsions incorporate hydrocarbon mols., whose concn. in the DMPC monolayers increases on going from the low-temp. (gel) to the high-temp. (liq. crystal) phase.

L17 ANSWER 9 OF 15 MEDLINE

DUPLICATE 7

ACCESSION NUMBER: 97354114 MEDLINE
DOCUMENT NUMBER: 97354114
TITLE: Cloning of the pumpkin ascorbate oxidase gene and analysis of a cis-acting region involved in induction by auxin.
AUTHOR: Kisu Y; Harada Y; Goto M; Esaka M
CORPORATE SOURCE: Faculty of Applied Biological Science, Hiroshima University, Higashi-Hiroshima, Japan.
SOURCE: PLANT AND CELL PHYSIOLOGY, (1997 May) 38 (5) 631-7.
Journal code: B1G. ISSN: 0032-0781.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-D55677
ENTRY MONTH: 199710
ENTRY WEEK: 19971003

AB A genomic clone encoding **ascorbate** oxidase was isolated from pumpkin (Cucurbita sp.). This gene is consisted of four exons and three introns. Analyses of the promoter fusion to beta-glucuronidase **reporter** gene by transient expression assay in pumpkin fruit tissues suggested the existence of a cis-acting region responsible for auxin regulation.

L17 ANSWER 10 OF 15 MEDLINE

DUPLICATE 8

ACCESSION NUMBER: 95155358 MEDLINE

DOCUMENT NUMBER: 95155358
TITLE: Ascorbic acid enhances iron-induced ferritin translation
in human leukemia and hepatoma cells.
AUTHOR: Toth I; Rogers J T; McPhee J A; Elliott S M; Abramson S L;
Bridges K R
CORPORATE SOURCE: Department of Medicine, Harvard Medical School, Brigham
and Women's Hospital, Boston, Massachusetts 02115.
CONTRACT NUMBER: HL 45794 (NHLBI)
AI 32717 (NIAID)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Feb 10) 270 (6)
2846-52.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199505

AB **Ascorbate** is an important cofactor in many cellular metabolic reactions and is intimately linked to iron homeostasis. Continuously cultured cells are **ascorbate** deficient due to the lability of the vitamin in solution and to the fact that daily supplementation of media with **ascorbate** is unusual. We found that **ascorbate** repletion alone did not alter ferritin synthesis. However, **ascorbate**-replete human hepatoma cells, Hep3B and HepG2, as well as K562 human leukemia cells achieved a substantially higher cellular ferritin content in response to a challenge with iron than did their **ascorbate**-deficient counterparts grown under standard culture conditions. Most of the elevation in ferritin content was due to an increase in de novo ferritin synthesis of greater than 50-fold, as shown by in vivo labeling with [35S]methionine and immunoprecipitation.

RNA-blot analysis showed only minor changes in steady state levels of ferritin mRNA, suggesting that **ascorbate** enhances iron-induced ferritin synthesis primarily by post-transcriptional events. Transient gene expression experiments using chloramphenicol acetyltransferase **reporter** gene constructs showed that the **ascorbate** effect on ferritin translation is not mediated through the stem-loop near the translational start site that transduces ferritin synthesis in response to cytokines. The data suggest that **ascorbate** possibly modifies the action of the iron-responsive element on ferritin translation, although more precise structure-function studies are needed to clarify this issue. These data demonstrate a novel role of **ascorbate** as a signaling molecule in post-transcriptional gene regulation. The mechanism by which **ascorbate** modulates cellular iron metabolism is complex and requires additional detailed investigation.

L17 ANSWER 11 OF 15 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95069071 EMBASE
DOCUMENT NUMBER: 1995069071
TITLE: Comparative analysis of ascorbate and AZT effects on HIV
production in persistently infected cell lines.
AUTHOR: Harakeh S.; Jariwalla R.J.
CORPORATE SOURCE: Virol Immunodeficiency Res Program, Linus Pauling Inst
Science Medicine, 440 Page Mill Road, Pale Alto, CA 94306,
United States
SOURCE: Journal of Nutritional Medicine, (1994) 4/4 (393-401).
ISSN: 0955-6664 CODEN: JNMEEU
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English

SUMMARY LANGUAGE: English

AB The effects of **ascorbate** (vitamin C) and azidothymidine (AZT) were examined on HIV expression in permanently infected and **reporter** cell lines. In T-lymphocytic HXB cells, constitutively producing moderate to high levels of virus, **ascorbate** suppressed HIV production and reduced the yield of infectious virus released into the culture supernatant. AZT, which has been reported to block de novo infection of freshly infected cells, did not inhibit constitutive virus production in HXB cells. In latently infected ACH-2 T-cells, producing low basal level of virus, exposure to phorbol ester (PMA) caused about 10-fold increase in virus production. Pre-treatment of ACH-2 cells with **ascorbate** followed by PMA stimulation resulted in a dose-dependent reduction in the extracellular level of HIV reverse transcriptase activity. AZT treatment did not suppress HIV activation in PMA-stimulated ACH-2 cells. In mixed cultures of uninfected HLCD4-CAT and infected HL2/3 cells, **ascorbate** did not affect virus-induced (tat-mediated) transcriptional activation of the CAT **reporter** gene linked to the HIV long terminal repeat. These results reveal anti-HIV effects of **ascorbate** that offer potential for development of combined therapy with other agents.

L17 ANSWER 12 OF 15 MEDLINE

DUPLICATE 9

ACCESSION NUMBER: 94251847 MEDLINE

DOCUMENT NUMBER: 94251847

TITLE: Mechanistic aspects of ascorbate inhibition of human immunodeficiency virus.

AUTHOR: Harakeh S; Niedzwiecki A; Jariwalla R J

CORPORATE SOURCE: Viral Carcinogenesis and Immunology Program, Linus Pauling Institute of Science and Medicine, Palo Alto, CA 94306.

SOURCE: CHEMICO-BIOLOGICAL INTERACTIONS, (1994 Jun) 91 (2-3) 207-15.

Journal code: CYV. ISSN: 0009-2797.

PUB. COUNTRY: Ireland

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199409

AB We have investigated the molecular basis of the inhibitory effect of **ascorbate** (vitamin C) on human immunodeficiency virus (HIV) expression in unstimulated chronically infected and **reporter** cell lines. Comparison of intracellular HIV RNA and protein patterns of **ascorbate**-treated cells with corresponding patterns of untreated controls, did not show significant differences in the synthesis or processing of individual viral RNA and polypeptides, indicating that the inhibitory effect of **ascorbate** is not directed at steps of viral transcription or translation. Enzyme assays on cell extracts showed that the activity of an HIV LTR-directed **reporter** protein made in **ascorbate**-treated cells was reduced to approximately 11% relative to that of untreated control. These results, combined with previous observations on the suppression of HIV RT activity, are consistent with a mechanism of action in which **ascorbate** exerts a posttranslational inhibitory effect on HIV by causing impairment of enzymatic activity.

L17 ANSWER 13 OF 15 MEDLINE

DUPLICATE 10

ACCESSION NUMBER: 94094826 MEDLINE

DOCUMENT NUMBER: 94094826

TITLE: Inactivation of phosphorylated rat tyrosine hydroxylase by ascorbate in vitro.

AUTHOR: Roskoski R Jr; Gahn L G; Roskoski L M

CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Louisiana

State University Medical Center, New Orleans 70119.

CONTRACT NUMBER: NS-15994 (NINDS)
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (1993 Dec 1) 218 (2)
363-70.
Journal code: EMZ. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199404

AB Tyrosine hydroxylase activity is reversibly controlled by the actions of several protein kinases. Previous studies showed that, following phosphorylation by protein kinase A, physiological concentrations of **ascorbate** irreversibly inactivate tyrosine hydroxylase. Several studies were performed to establish the mechanism of inactivation. We found that inactivation occurred under oxygen-free conditions. The results

of this and other experiments suggest that oxygenated species such as superoxide or hydrogen peroxide were not required for inactivation by **ascorbate**. Inhibition of tyrosine hydroxylase by low concentrations of **ascorbate** raised the question concerning the mechanism for maintaining enzyme activity under physiological conditions. We report that tyrosine, N alpha-methyl tyrosine, 3-iodotyrosine, and phenylalanine protected the phosphorylated enzyme against **ascorbate** inactivation. Catecholamines (dopamine, norepinephrine, and some of their analogues) also protected the enzyme against **ascorbate** inactivation. We performed studies to assess conformational changes of tyrosine hydroxylase by measuring the extrinsic fluorescence using 8-anilino-1-naphthalenesulfonic acid as a **reporter** group. Phosphorylation of tyrosine hydroxylase by protein kinase A decreased the extrinsic fluorescence. Treatment of tyrosine hydroxylase with **ascorbate** produced a further decrease in fluorescence. These results provide evidence for conformational changes following these treatments. In contrast to extrinsic fluorescence, the circular dichroic spectrum of tyrosine hydroxylase failed to change following phosphorylation by protein kinase A or inhibition by **ascorbate**. The spectrum was consistent with a secondary structure of tyrosine hydroxylase with 55% alpha helix, 20% beta sheet, 2% beta turn, and 23% random coil.

L17 ANSWER 14 OF 15 MEDLINE DUPLICATE 11

ACCESSION NUMBER: 87100946 MEDLINE
DOCUMENT NUMBER: 87100946
TITLE: DNA cleavage specificity of a group of cationic metalloporphyrins.
AUTHOR: Ward B; Skorobogaty A; Dabrowiak J C
CONTRACT NUMBER: GM31895 (NIGMS)
SOURCE: BIOCHEMISTRY, (1986 Nov 4) 25 (22) 6875-83.
Journal code: A0G. ISSN: 0006-2960.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198705

AB The ability of a group of water-soluble metalloporphyrins to cleave DNA has been investigated. Incubation of Mn³⁺, Fe³⁺, or Co³⁺ complexes of meso-tetrakis(N-methyl-4-pyridiniumyl)porphine (H₂T4MPyP) with DNA in the presence of **ascorbate**, superoxide ion, or iodosobenzene results in DNA breakage. Comparisons between the rates of porphyrin autodestruction with the rates of strand scission of covalently closed circular PM2 DNA indicate that the porphyrins remain intact during the cleavage process. Analysis of the porphyrin-mediated strand scissions on

a

139-base-pair restriction fragment of pBR322 DNA using gel electrophoresis/autoradiography/microdensitometry reveals that the

minimum

porphyrin cleavage site is (A X T)₃. The cleavage pattern within a given

the site was found to be asymmetric, indicating that porphyrin binding and strand scission process are highly directional in nature. In addition to an analysis of the mechanism of porphyrin-mediated strand breakage in terms of the DNA cleavage mechanism of methidium-propyl-iron-EDTA and Fe-bleomycin, the potential of the cationic metalloporphyrins as footprinting probes and as new "**reporter** ligands" for DNA is presented and discussed.

L17 ANSWER 15 OF 15 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 76058372 EMBASE
DOCUMENT NUMBER: 1976058372
TITLE: Mercuri nitrophenol as a reporter group for the conformational change of hemoglobin.
AUTHOR: Yagisawa S.
CORPORATE SOURCE: Dept. Biophys. Biochem., Fac. Sci., Univ. Tokyo, Japan
SOURCE: Journal of Biochemistry, (1975) 77/3 (595-604).
CODEN: JOBIAO
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
029 Clinical Biochemistry
025 Hematology
LANGUAGE: English

AB One mole of horse hemoglobin tetramer reacts with 2 moles of 2 chloromercuri 4 nitrophenol (MNP) at .beta.93 cysteine. The difference spectra between MNP bound hemoglobin and hemoglobin, measured with the aid of ascorbic acid and **ascorbate** oxidase [EC 1.10.3.3] as deoxygenation reagents, indicate that the pK of the phenolic hydroxyl group of MNP increases by 0.6 to 0.8 pH unit on deoxygenation of the hemoglobin. The Hill constant of the modified hemoglobin changes with pH. It decreases from about 2.4 at pH 6.8 to about 1.0 at pH 9.0. This effect of the reagent is interpreted as inherent to the **reporter** groups.

=> s yiaJ and ascorbate

L18 1 YIAJ AND ASCORBATE

=> d l18 ibib abs

L18 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:260592 CAPLUS
DOCUMENT NUMBER: 132:289575
TITLE: Metabolic selection methods and their application to the yiaK-S operon from Klebsiella oxytoca
INVENTOR(S): Hoch, James; Dartois, Veronique
PATENT ASSIGNEE(S): Microgenomics, Inc., USA
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2000022170	A1	20000420	WO 1999-US23862	19991012
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9964297	A1	20000501	AU 1999-64297	19991012
PRIORITY APPLN. INFO.:			US 1998-172952	19981014
			WO 1999-US23862	19991012

AB The present invention relates in part to methods for screening for novel enzymic pathways in environmental samples using metabolic selection strategies, and the isolation of the genes and proteins that make up these pathways. A metabolic selection strategy is designed to find an enzymic pathway for the conversion of any source compd. to any target compd. The invention features a method of screening for one or more nucleic acid sequences which express a product or products that convert a source compd.

into a target. compd. The method comprises contacting a cell with one or more test nucleic acid sequences, where the cell expresses one or more genes encoding one or more proteins which, in the presence of the target compd., provide a detectable signal. The detectable signal indicates the presence of the desired nucleic acid sequence or sequences. Conservatively, this technique allows at least a million-fold increase in the discovery rate over classical biochem. screening approaches, and allows testing of the 99% of environmental microbes that are currently unable to be cultured in the lab. The metabolic selection technique is exemplified by the identification, phys. mapping, and sequence anal. of the Klebsiella oxytoca yiaK-S operon, responsible for the metabolic pathway of 2-keto-L-gulonate to ascorbic acid.

REFERENCE COUNT:

2

REFERENCE(S):

- (1) Blatter; The Complete Genome Sequence of Escheria coli 1997, V277, P1453
- (2) Thompson; US 5824485 A 1998 CAPLUS

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Executing the logoff script...

=> LOG H

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	130.48	130.63
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-5.01	-5.01

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 15:46:42 ON 11 DEC 2000